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THE PERIPHERAL ACTION OF DIGOXIN ON VENOUS PRESSURE: A STUDY USING SHEEP WITH AN "ARTIFICIAL HEART".[1]

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THERE seems no sign in recent literature that a direct peripheral action of digitalis upon venous pressure is generally accepted. Wilson and Schild (1952) state that it is more probable that digitalis improves the contractility of the heart in the first instance, and that changes in venous pressure "are largely a consequence of this action".

It is the purpose of this paper to show that therapeutic concentrations of digoxin can alter inferior *vena cava* pressure in sheep with an "artificial heart", when, clearly, any possible myocardial effect can be excluded. It is not suggested that this direct peripheral action of digoxan upon venous pressure is the principal action of the drug, but merely that in sheep it exists as a factor and should thus be considered in the integration of the many effects which digoxin can have upon the animal with an intact circulation.

[1] This research was aided by a grant from the Kahn Fund of the University of Sydney, and by a grant from the National Health and Medical Research Council of Australia.

Double Perfusion Pump and Oxygenator and its Use.

Perfusion of the entire dog in non-survival experiments was described in 1942 by de Burgh Daly and his co-workers. They used the preparation to study pulmonary vasomotor fibres and also reviewed similar but less elaborate preparations made by earlier workers. More recently, in relation to cardiac surgery, a great deal of attention has been given to the development of mechanical pump-oxygenators in order that temporary replacement of the heart and lungs of animals may be effected and yet be followed by prolonged survival of the animal in a healthy condition; in one instance this has been applied to a human subject (Dennis *et alii*, 1951). Two publications (Dennis *et alii*, 1951; Miller *et alii*, 1951) in October, 1951, give access to the principal literature on this subject.

The double perfusion pump and oxygenator to be described is used to maintain (at constant or varying rates) the pulmonary and systemic circulations of sheep. It is seen in Figures I and II and has the advantage of being a single mobile unit.

The chassis of the double perfusion pump and oxygenator is made of cast brass (upper part), fabricated steel (pedestal) and welded angle iron. The two synchronous pumps are driven by a quarter horse-power, series connected, direct current motor (A). The motor is coupled by V-belts to the main driving shaft, which imparts a fixed thrust to a sliding rod (B). A variable proportion of this thrust is transmitted to another sliding rod (C) by means of a connecting rod (D), the fulcrum of which is movable by means of a small crank-handle (E). The stroke-volume of the sylphon bellows (F) can thus be varied at will. The sylphon bellows are hydraulically coupled to a thick-walled "Perspex" chamber (G). As water from the sylphon

bellows enters and leaves the "Perspex" chamber, blood is driven out of and drawn into the balloon (H), directional flow being imparted by rubber valves in the valve assembly (I). This is the Dale-Schuster principle (Dale and Schuster, 1928) modified. An air-trap is connected to the top of each valve assembly. The rate of the pump is controlled by varying the voltage input of the electric motor by means of the rheostat (J). Three-way glass taps (K) allow circulation of blood or saline prior to cannulation of the animal from glass reservoirs (L) through the pumps and back to the reservoirs, or after cannulation from the reservoirs through the pumps to the animal; the blood from the animal then returns via the atrial cannulæ to the reservoirs. The reservoirs are immersed in a water bath thermostatically controlled at 37° C.

A "Perspex" blood-oxygenator (M) of the Hooker (1915) and Drinker (Drinker *et alii*, 1922) type is mounted on the top of the pump chassis. Blood is pumped up from the systemic venous reservoir by means of a single, modified Dale-Schuster pump unit (N), and enters the top of the oxygenator (O); this blood is then spun out to the sides of the "Perspex" chamber by a spinning "Perspex" disk driven by a belt from the main driving shaft. As the film of blood flows down the sides of the "Perspex" chamber it is equilibrated with a mixture of 95% oxygen and 5% carbon dioxide, which is continuously being passed through the oxygenator; this blood is returned to either of the venous reservoirs by a rubber tube leading from the bottom of the oxygenator. The temperature of the blood in the oxygenator is maintained at approximately 37° C. by means of a carbon filament lamp (P) fitted into the bottom of the "Perspex" chamber. (The Dale-Schuster pump unit used for the oxygenator is standard equipment manufactured by C. F. Palmer, London, Limited.)

After cannulation of the animal blood flows from the right and left atria to the systemic venous and pulmonary venous reservoirs along rubber tubes from the atrial cannulæ (Q), and enters the reservoirs through a J-tube open to the atmosphere (see Figure III). This "fixes" central venous pressure at zero (atmospheric) pressure in a given horizontal plane. The whole of the upper part of the chassis (including the reservoirs and the J-tubes) can be raised or lowered by means of a screwjack and hand wheel (R).

The pumps are calibrated statically, and dynamically against varying pressures. The rate per minute of the pumps can be read off on a dial below the sliding rod (C), while stroke volume can be read off from a scale along which slides the fulcrum of the connecting rod (D). The pulmonary artery and aortic pumps are capable of outputs of five litres of blood per minute and more, against pressures of up to and greater than 200 millimetres of mercury. The accessory Dale-Schuster pump for the oxygenator is usually set at about 0·6 to 0·7 litre per minute, and at this rate damage to the red blood cells in the oxygenator is minimal. The animal's own lungs are used to oxygenate the blood, and the oxygenator is merely an adjunct to ensure full oxygenation of the systemic arterial blood. A slight amount of frothing of the blood occurs in the oxygenator, but as this floats on top of the blood in the reservoir it can be sucked off and discarded from time to time.

Outline of Surgical Technique.

The sheep chosen for the experiments weighed approximately 60 pounds. As the experiments are non-survival ones, aseptic technique is not essential.

Anæsthesia.

In the initial stages the animal is anæsthetized by the intravenous injection of "Nembutal" (5% solution) until the rib resection is completed; further anæsthetic is added as necessary in the form of the long-acting sodium barbitone (10% solution), to keep the animal at the level of light surgical anæsthesia.

Blood Transfusion.

The left external jugular vein is exposed and a straight polythene catheter (of about four millimetres bore) inserted therein for several centimetres. A slow transfusion of pooled donor sheep blood is thus commenced at the outset.

Artificial Respiration.

Tracheotomy is then performed. A flanged glass cannula is tied into the trachea and connected to a Starling's ideal respiratory pump (Starling, 1926), artificial respiration being maintained by positive pressure insufflation. The respired air is enriched with oxygen bubbled through warm water. A side tube on the tracheal cannula allows mucus to be sucked out of the trachea without discontinuance of the artificial respiration.

Thoracotomy and Pericardotomy.

The fourth and fifth left ribs are removed subperiosteally from as far posteriorly as possible to the costochondral junctions. The third left rib is completely fractured subperiosteally and the pleura is opened. The exposed left lung is immediately covered with thin dental dam rubber moistened in warm physiological saline, and rubber-covered Shelden's rib retractors are inserted into the pleural cavity. Five millilitres of 5% procaine solution are next injected into the pericardial sac. After about five minutes the pericardial sac is opened by a cruciate incision and the four flaps are sewn to the edges of the thoracotomy wound, a pericardial cradle being formed. The two posterior pericardial flaps also serve to shut off the rubber-covered left lung from the operative field. Both atria, the pulmonary artery and the ascending aorta are accessible by this left-sided approach. Two guide tapes each are placed around the pulmonary artery and the ascending aorta preparatory to cannulation of these vessels. The tapes are half an inch wide and moistened in warm saline solution.

Catheterization of the Inferior Vena Cava.

If the right index finger is placed around the inferior *vena cava* in the pericardial sac, the catheter in the external jugular vein can almost always be guided into the inferior *vena cava* for 20 to 25 centimetres. (The position of the catheter tip is checked *post mortem* at the end of the experiment.) The animal is then given 25,000 to 30,000 international units of heparin via the catheter.

Cannulation of Atria and Great Vessels.

A cannula filled with warm saline is inserted into the right atrium through the auricular appendage while the appendage is temporarily clamped off from the atrial cavity by a rubber-covered, non-crushing clamp. The cannula is tied in with half-inch wide tape, moistened with warm saline. The transfusion of donor blood is then accelerated and a clamp on the rubber tubing from the right atrial cannula to the systemic venous reservoir is partly released to allow blood from the right atrium to trickle into the reservoir at about the same rate as the donor blood is being transfused into the inferior *vena cava*. Thus the reservoir is gradually filled up to the 500 millilitre mark with the recipient sheep's blood and an admixture of donor blood which has been circulating through the animal; this avoids the drastic vasopressor effect which the sudden addition of a large quantity of foreign donor blood (when perfusion starts) usually has. The pumps are then started to allow circulation of the blood throughout its parts, through the oxygenator and back to the reservoir.

The pulmonary artery is next clamped with rubber-covered Harrison Cripp's forceps as close to the right ventricle as possible, the artery is incised, a cannula is tied into the distal cut end, the pulmonary artery pump is started with the three-way tap directing blood flow to the animal, and the clamp is removed from the right atrial tubing leading to the systemic venous reservoir. This procedure needs five pairs of hands trained to act as a team, and can be accomplished in sixteen to twenty-five seconds, by the use of the two guide tapes already around the artery, two pairs of Duval's intestinal and lung

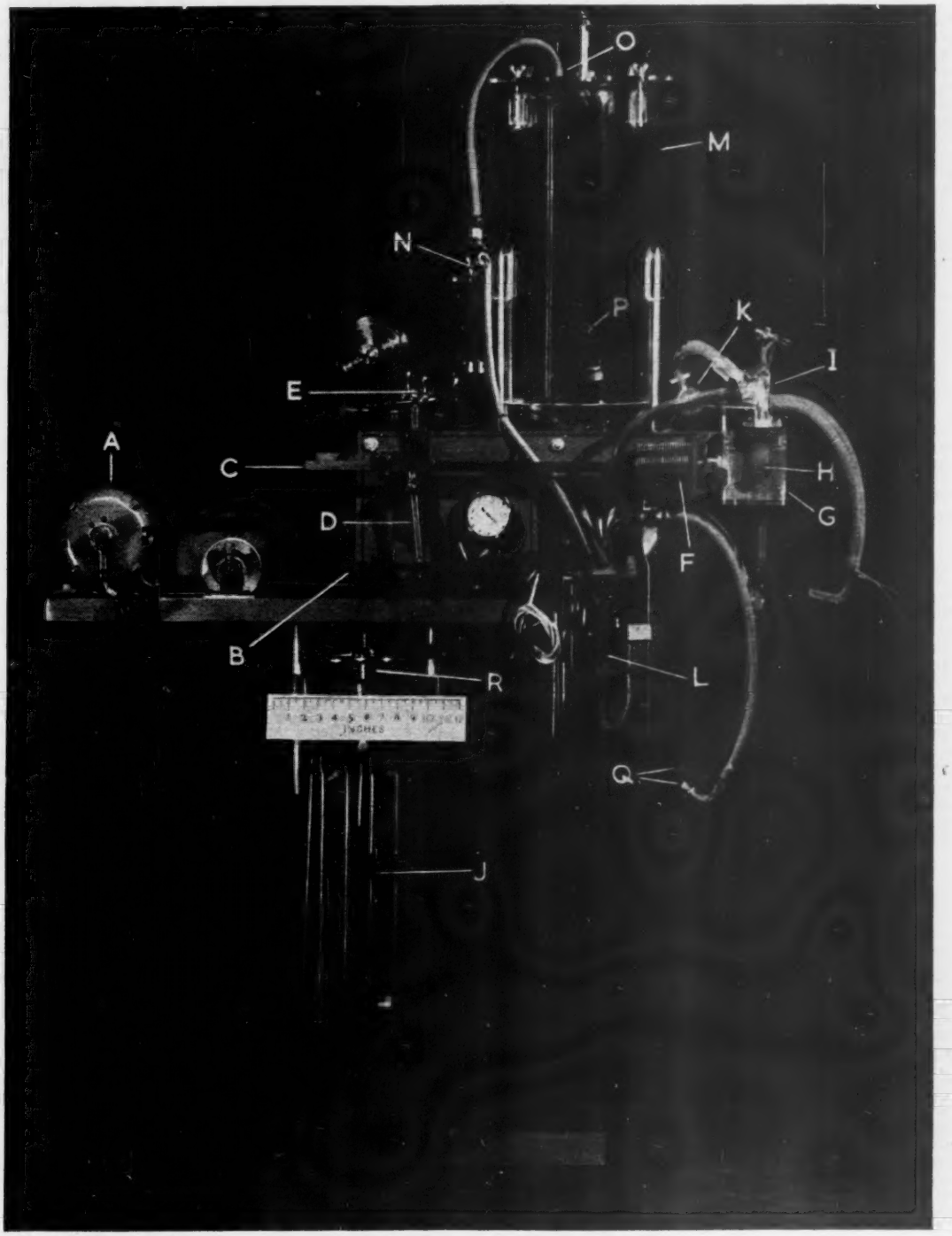

FIGURE 1.

The double perfusion pump and oxygenator seen from one side. The pulmonary artery pump, but not the aortic pump, is visible from this view. See text.

forceps and a special knotting frame. Arrest of the circulation for this period of time seems in itself to have little ill-effect afterwards. The right ventricle is now by-passed, its outflow tract is clamped and systemic venous blood collected from the right atrium is artificially pumped via the pulmonary artery through the animal's lungs. The animal's heart continues to beat, the left side of the heart adapting itself to and dealing with the blood pumped artificially through the lungs. The desired rate of perfusion of the lungs can be gauged by observing the left auricle, so that this chamber is neither collapsed and inadequately filled during diastole nor overdistended during this period. This usually means a perfusion rate between two and three litres of blood per minute.

The left atrium is then cannulated and blood allowed to trickle into the pulmonary venous reservoir at the same rate as the blood transfusion, which is again quickened. The pulmonary venous reservoir is partly filled with blood, which is allowed to circulate through the aortic pump and back to the reservoir. The ascending aorta is then clamped close to the left ventricle, the coronary supply to the heart being cut off. The aorta is then incised and cannulated (as in the case of the pulmonary artery), so that pulmonary venous blood collected from the left atrium is now pumped into the aorta. Both ventricles are now by-passed, both pulmonary and systemic circulations being maintained by the double perfusion pump. Within a few minutes the animal's own heart ceases to beat as its coronary flow has ceased. The "dead" heart is allowed to remain *in situ* to act as a passive collecting chamber for systemic venous and pulmonary venous blood; functionally it is replaced by the double perfusion pump.

Comment.

Some 20 perfusion experiments have been successfully made, the animal's corneal reflex being present for one and a half to five hours after replacement of the animal's own heart by the perfusion apparatus. The blood vessels have been pharmacologically reactive to numerous drugs during this period. Furthermore, when perfusion and respiratory pumps are switched off at the end of an experiment, the following occur: (i) loss of the corneal reflexes within two to five minutes; (ii) dilatation of a previously moderately small pupil; (iii) independent gasping respirations; (iv) convulsive muscular movements.

Sixty-pound sheep were usually perfused at a rate of two and a half to three litres of blood per minute, the exact perfusion rate being adjusted so as to produce a mean systemic blood pressure of 100 to 110 millimetres of mercury.

Results of Digoxin Experiments.

Mean aortic pressure was recorded on smoked paper and kymograph by a mercury manometer connected to the side tube of the aortic cannula. Mean inferior *vena cava* pressure was recorded 20 to 25 centimetres from the diaphragmatic orifice of the inferior *vena cava* by means of a straight polythene catheter (of about four millimetres' bore) connected to a recording saline manometer, which also writes on the kymograph; the position of the catheter tip was checked *post mortem* at the end of each experiment.

Perfused Sheep.

In four sheep which were artificially perfused at a constant rate under sodium barbitone anæsthesia, 0·8 milligramme of digoxin diluted in saline was injected into the systemic venous reservoir. As the normal blood volume of these sheep was increased by blood in the extracorporeal circuit (reservoirs, pumps, tubing, oxygenator), which amounted to about one and a half litres, 0·8 milligramme of digoxin in such 60 pound sheep would be in the vicinity of the ordinary full, therapeutic, digitalizing dose. In each case a rise of mean pressure occurred in the inferior *vena cava* after the addition of the digoxin. (See Figure IV and Table I.) A slight narrowing of the aortic tracing also occurred in each case as evidence of slight arteriolar constriction. While the inertia of the mercury column in the mercury manometer allows no indication of the actual systolic, diastolic and pulse pressures, the tracing is a reliable gauge of mean aortic pressure and of directional changes in the pulse pressure. Arteriolar constriction produced by digitalis has been recognized for many years (Cushny, 1925).

Control Sheep.

In four normal control sheep with intact circulations, weighing about 60 pounds and also under sodium barbitone anæsthesia, a polythene catheter (of about four millimetres' bore) was passed via the exposed left external jugular vein into the right atrium. The catheter was connected to a recording saline manometer writing on smoked paper and kymograph. The catheter was passed without X-ray control, the principle mentioned by Wood being used (Wood and Paulett, 1949). To make certain that the catheter tip was in the right atrium, the right ventricle was always entered first and the catheter was then withdrawn slowly till an abrupt fall of pressure occurred and the large ventricular pulsations disappeared. An amount of 0·7 milligramme of digoxin diluted in saline was later injected into a leg vein which had been exposed previously and cannulated for a very slow intravenous drip infusion of glucose (5%) in one-fifth normal physiological saline. In three control sheep the mean right atrial pressure showed no significant change after the intravenous injection of digoxin, while in one sheep the mean right atrial pressure fell slightly. (See Figure V and Table II.)

Reference Level.

In all experiments the reference level for all pressure determinations was the mid-thoracic vertebral spines with the animal lying on its right side. X-ray photographs of normal sheep in this position show that the centre of the right atrium would be about three to four centimetres below this reference level.

Discussion.

McMichael (1950), reviewing concepts of heart failure, points out that, while there has been a good deal of evidence in the literature that digitalis produces a slight venous pressure fall in normal animals and in man, this occurrence is now recognized as being much less constant than was originally thought. The findings described in the present paper by the use of control normal sheep under sodium barbitone anæsthesia are in keeping with this view; in three such sheep a continuous record of mean right atrial pressure showed no significant change after the intravenous injection of digoxin, at least for periods of one to one and a half hours, while in one sheep the mean right atrial pressure fell approximately two centimetres of saline.

The pharmacological evidence that digitalis and allied drugs increase cardiac contractile power in certain circumstances is overwhelming and will not be reviewed here. On the other hand, the earlier observations (Kaufmann, 1884) of diminished cardiac output in normal animals after the administration of digitalis have been amply confirmed (Harrison and Leonard, 1926; Dock and Tainter, 1930; Stewart and Cohn, 1932; Ryland, 1933; McMichael and Sharpey-Schafer, 1944). Dock and Tainter (1930) first suggested that an action of digitalis on peripheral vasculature might explain the reduced cardiac output produced in normal animals by the drug. They adduced evidence that digitalis constricted the hepatic veins in dogs, damming back blood in the liver and spleen, so reducing venous return and venous filling pressure of the heart. Thus they explained the fall in cardiac output produced in normal animals by digitalis. Katz and others (1938) strongly supported this hypothesis. However, Wood in 1940 demonstrated in a patient with congestive heart failure that after the administration of digoxin, and coincidently with the fall of venous pressure, the liver and spleen decreased in size; it followed that in this case the fall in venous pressure could not be due to hepatic venous constriction or portal venous constriction above the mouth of the splenic vein.

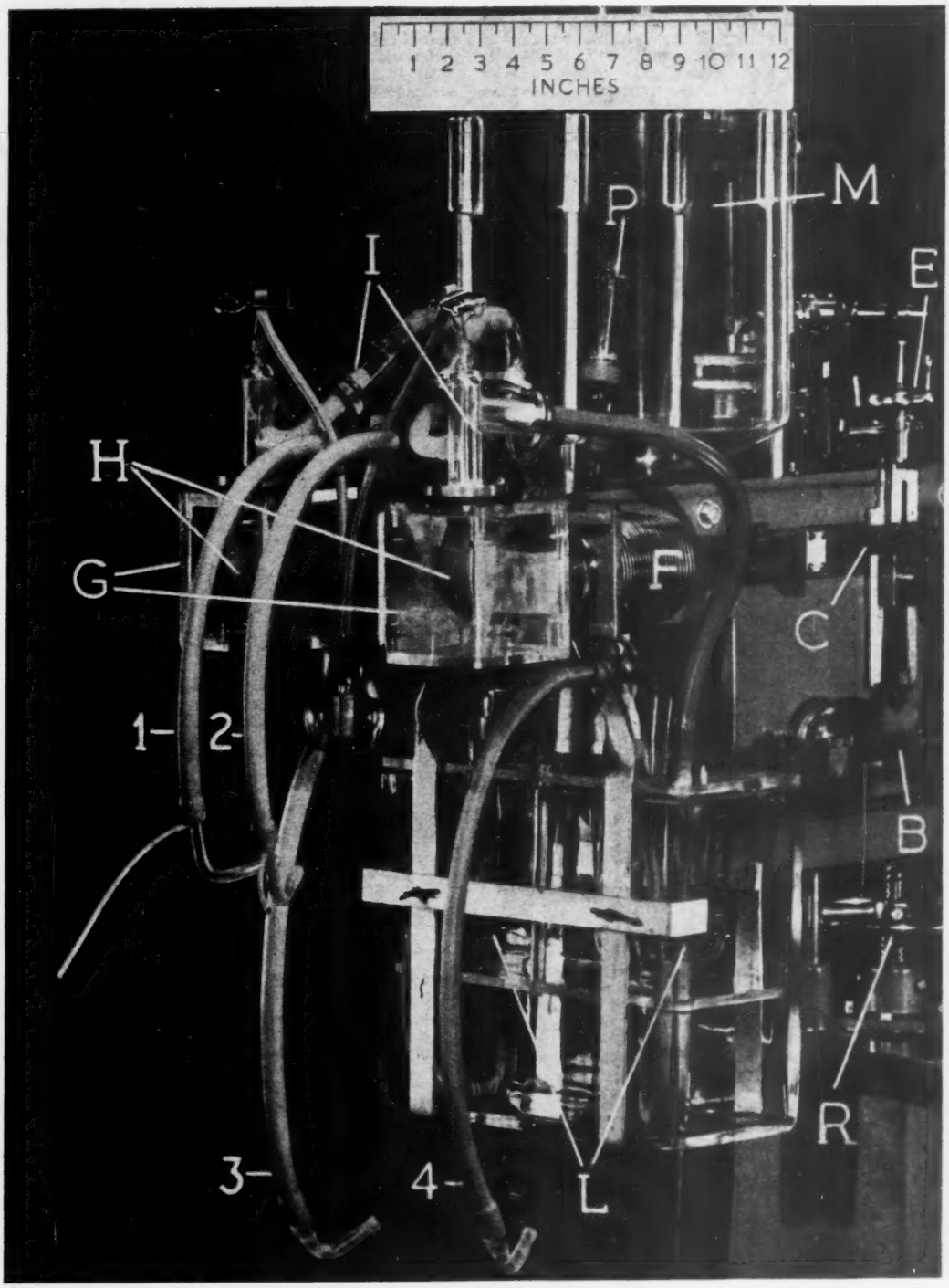

Figure II.

Portion of the double perfusion pump and oxygenator seen obliquely from the front. The pulmonary artery and aortic pumps are both visible. The figures 1, 2, 3 and 4 respectively designate the tubing and cannulæ for the pulmonary artery, aorta, right atrium and left atrium. The cannulæ are made of "Perspex", the tubing is of rubber, while the pulmonary artery and aortic cannulæ have side tubes to allow for the recording of pressures.

The notion of a primary action of digoxin upon venous pressure was revived by McMichael and Sharpey-Schafer in 1944, it being suggested that the cardiac effects of digoxin were secondary to a primary peripheral action of digoxin which reduced venous pressure. This hypothesis was neither accepted nor completely disproved by Cournand and others in 1949; the hypothesis was then withdrawn in 1950 by McMichael himself: "Since primary venous pressure reduction can no longer be invoked to explain the variety of cardiac output responses to digitalis, it is necessary to account for venous pressure reduction in the absence of cardiac output increase in some other way."

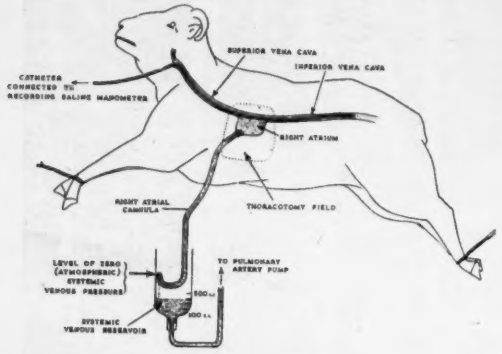

FIGURE III.

Diagram of portion of perfusion circulation. In the perfusion experiments blood is returned from the right and left atria (by cannulæ inserted through the auricular appendages) to systemic venous and pulmonary venous reservoirs respectively. Blood from these reservoirs is pumped by the double perfusion pump into the pulmonary artery and aorta at constant perfusion rates. The animal's heart is thus completely replaced from a functional point of view and no longer beats, as its coronary circulation has been arrested. The diagram shows the following details. (i) The right atrial cannula is connected to the systemic venous reservoir, the blood which flows into the reservoir being open to the atmosphere; central systemic venous pressure is thus "fixed" at zero (atmospheric) pressure. (ii) A polythene catheter is tied into the left external jugular vein, has its tip in the abdominal part of the inferior *vena cava*, and is connected to a recording saline manometer. Blood leaves the systemic venous reservoir at a constant rate, so that if this reservoir level is constant, the total blood flow through the *venæ cavæ* (into the reservoir) must be constant. Under these conditions a rise of pressure in the inferior *vena cava* produced by digoxin is clearly a peripheral effect, since central venous pressure is "fixed" at zero.

In the present series of experiments described on artificially perfused sheep the following conditions were established: (i) the pulmonary and systemic circulations were perfused at a constant rate; (ii) total blood flow through the *venæ cavæ* into the systemic venous reservoir was constant (since the reservoir level was constant and blood was leaving the reservoir at a constant rate); (iii) cardiac action on venous pressure was excluded since the heart was "dead" and not beating, its coronary flow having been arrested an hour or more previously; the "dead" heart was merely left *in situ* to serve as a passive collecting chamber to collect systemic venous and pulmonary venous blood via the atria; as a further check two white spots painted on the heart showed no alteration of the intervening distance during the experiment, indicating no alteration in the size of the "dead" heart chambers; (iv) central venous pressure was fixed at zero by having the atrial cannulæ open to the atmosphere on a selected horizontal plane. Under these conditions, it is considered, the rise of mean pressure in the lower part of the inferior *vena cava* produced by digoxin can be due only to a peripheral action of the drug upon venous pressure. The cause of the rise of pressure in the lower part of the inferior *vena cava* would seem to be one or other of the following; (*a*) a slight general venoconstriction along the length of the inferior *vena cava*, increasing slightly the gradient of pressure fall along this portion of the venous system from the periphery; (*b*) a more localized sphincter-like venoconstriction of the upper part of the inferior *vena cava* (contrast Dock and Tainter's hepatic vein constriction); (*c*) a theoretical possibility, considered unlikely but not as yet excluded, that while total *vena cava* blood flow was known to be constant, digoxin might have selectively caused a diminished blood flow along the

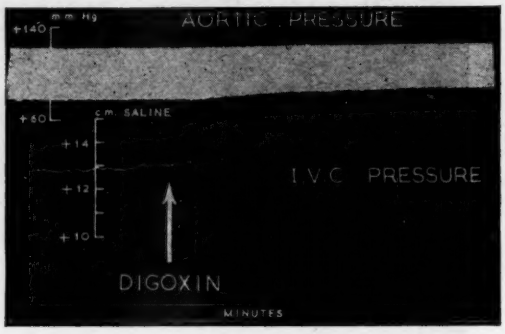

FIGURE IV.

Experiment on a sheep whose heart had been completely replaced functionally by a double perfusion pump which perfused the pulmonary and systemic circulations at a constant rate. The animal was under sodium barbitone anæsthesia. The tracings show that after the addition of digoxin to the systemic venous reservoir there is a rise in mean inferior *vena cava* pressure of approximately two centimetres of saline, while slight narrowing of the aortic tracing is evidence of slight arteriolar constriction.

superior *vena cava* and an increased blood flow along the inferior *vena cava*, the latter producing the increase in inferior *vena cava* pressure.

If either (*a*) or (*b*) was the case, digoxin would have a direct peripheral action, increasing the gradient of pressure fall along the inferior *vena cava*, apart of course from any direct action on the myocardium, which latter effect might frequently obscure the former in an animal

TABLE I.

Effect of Administration of Digoxin on Mean Inferior Vena Cava Pressure in Artificially Perfused Sheep (Under Sodium Barbitone Anæsthesia).

Perfused Sheep.	Approximate Rise of Pressure (to Nearest 0·5 Centimetre of Saline).	Time Taken for Rise of Pressure to Begin.	Time Taken for Full Effect.
Sheep I ..	3·0 centimetres.	10 to 12 minutes.	1 hour 20 minutes.
Sheep II ..	1·5 centimetres.	6 to 8 minutes.	40 minutes.
Sheep III ..	2·0 centimetres.	4 to 6 minutes.	25 minutes.
Sheep IV ..	3·5 centimetres.	8 to 10 minutes.	Pressure was still rising (though much more slowly) after 2 hours.

with an intact circulation. The fact that in any case a peripheral action of digoxin on venous pressure can be demonstrated (in sheep artificially perfused at a constant rate and with central venous pressure fixed at zero) is not to suggest that the principal action of digoxin in intact sheep is on venous pressure; in the control sheep with intact circulations continuous records of mean right atrial pressure for one to one and a half hours after the intravenous injection of digoxin showed no significant change in three sheep, and a fall in pressure of two centimetres of saline in one sheep. It is well known that cardiac adaptation to varying venous inflow is a most

important factor tending to stabilize venous pressure (Eyster, 1929).

Summary and Conclusions.

A double perfusion pump capable of maintaining, at constant or varying rates, the pulmonary and systemic circulations of anæsthetized sheep is described.

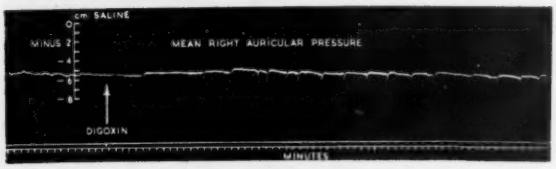

FIGURE V.

Control experiment using a sheep with an intact circulation and also under sodium barbitone anæsthesia. The tracing shows that the intravenous administration of digoxin does not significantly alter mean right auricular pressure, at least for a period of up to one hour. The downward spikes on the tracing are due to occasional sighing inspirations superimposed on the ordinary respiratory rhythm.

In each of four sheep whose hearts had been replaced functionally by the double perfusion pump which perfused the pulmonary and systemic circulations at constant rates, addition of digoxin to the systemic venous reservoir was followed by a rise of pressure in the inferior *vena cava*. This seems unequivocal evidence of the existence of a peripheral action of digoxin upon venous pressure. In four control sheep with intact circulations and under the same anæsthetic, the intravenous injection of digoxin caused either no alteration or a slight fall of mean right atrial pressure. These findings are discussed in relation to recent literature on the subject.

TABLE II.

Effect of Administration of Digoxin on Mean Right Atrial Pressure in Control Sheep with Normal Intact Circulations (Under Sodium Barbitone Anæsthesia)

Control Sheep.	Change in Mean Right Atrial Pressure During Periods of Not Less than One Hour After Administration of Digoxin.
Sheep I ..	No significant change.
Sheep II ..	No significant change.
Sheep III ..	Fall of approximately 2·0 centimetres of saline, commencing 8 to 10 minutes after administration of digoxin, falling to a minimum in about 50 minutes, and persisting for the period of 1 hour 40 minutes, during which the recording was continued.
Sheep IV ..	No significant change.

Acknowledgements.

I am greatly indebted to Professor C. G. Lambie for continued advice and encouragement during this perfusion work, to Professor H. R. Dew for advice regarding surgical principles involved, and to Mr. D. H. Cohen, M.S., F.R.A.C.S., for assistance in developing the surgical technique in the early experiments. Thanks are due to Mr. F. Boland, and later Mr. P. Lawson, in conjunction with whom the double perfusion pump was designed, manufactured and calibrated in the Department of Medicine, University of Sydney. Thanks are especially due to Mr. R. Dunphy, Mr. W. Muir, Mr. P. Lawson, Mr. W. Green, Mr. D. Fahey and Mr. H. Williams for their ever-willing assistance in the laboratory during perfusion experiments. Without this help none of the perfusion experiments could have been carried out. I wish to thank Mr. Handel, of the Sydney Meat Preserving Company, for his cooperation in procuring suitable sheep for us, and for allowing us to collect donor sheep blood from the Sydney Meat Preserving Company killing yards. I wish also to thank Mr. F. Hamilton, of the McMaster Laboratories, Commonwealth Scientific and Industrial Research Organization, for lending us sheep for the cardiac catheterization (control) experiments, and for allowing us to yard our sheep for the perfusion non-survival experiments in the McMaster yards. Lastly, I wish to thank Mr. R. Dunphy for the drawing, and Mr. Woodward-Smith for the photographs.

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SPATIAL VECTORELECTROCARDIOGRAPHY: THE TECHNIQUE AND THE NORMAL VECTORELECTROCARDIOGRAM.

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IN electrocardiography the heart's electrical activity is recorded from two or more electrodes placed on body surfaces. This activity is usually portrayed with voltage set against time and is a record only of the electrical activity between those lead-off points.

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The lead-off points in common use are the right arm, the left arm and the left leg leads described by Einthoven, giving the standard leads I, II and III, and many "unipolar" leads placed across the precordium, on limbs or in the œsophagus.

In any consideration of the heart's electrical activity it must be remembered that the heart is a three-dimensional structure, and on the presumption that its electrical activity occurs in three dimensions, any specification of its total "manifest" electrical activity must be made in three dimensions. Such a three-dimensional specification involves synthesis of records obtained from various leads situated in several planes through the body. Whilst this synthesis has often been made by graphic or mathematical methods, it has been until recent years only of academic interest, because of the labour involved in making it.

In general, clinicians use a standard set of leads and interpret them in the light of the known variations in health and disease which have been empirically determined for each lead. This necessitates knowledge of the normal values for each lead used.

However, in recent years developments in electronic apparatus have made possible the construction of apparatus to make this synthesis automatically and the portrayal of the result on a fluorescent screen which can be photographed for permanent record.

If it can be shown that the synthesized picture of the heart's "manifest" electrical activity contains all the information present in the traditional leads, then a method is available which reduces to very small numbers the tracings necessary for the investigation of any one case. The number of normal standards to be learnt and the chances of faulty interpretation are correspondingly reduced.

The term "spatial vectorelectrocardiography" has been applied to the synthesis and use of this three-dimensional picture, whether obtained graphically or electrically.

In this paper an account is given of the technique of vectorelectrocardiography and of the records from a series of 104 normal individuals.

Technique.

A study of any electrocardiogram shows that the heart's electrical activity varies in intensity with the passage of time, and a synthesis from various leads shows that the direction of this activity also varies with time. Such a quantity which possesses both direction and magnitude is termed a vector quantity, and so the term vectorelectrocardiography is derived.

Einthoven (1913) showed that, with respect to records obtained from the right arm, the left arm and the left leg (leads I, II and III), the heart's electrical activity could be represented approximately as a small source of electricity in a uniformly conducting plane sheet of material, and that the three points (RA, LA, LL) behaved as though they were at the apices of an equilateral triangle in that plane.

The drawing in Figure I indicates how, if this is true, vector analysis relates and synthesizes, at any instant, the electrical activity in leads I, II and III into a vector in that plane. In Figure II this procedure is applied at successive instants throughout the cardiac cycle, and produces a frontal plane vectorelectrocardiogram. It is apparent that the closed loops represent the path inscribed by the movement of the free end of the vector about the cardiac electrical centre, and correspond to the *P*, *QRS* and *T* complexes of the cycle.

The introduction by Wilson in 1941 of unipolar limb leads (V_R, V_L, V_F), and the modified leads introduced by Goldberger in 1942 (aV_R, aV_L, aV_F), provide further records of potential changes in the frontal plane. These leads produce three further axes for the analysis or synthesis of the "manifest" cardiac vector in the frontal plane.

Wilson, in 1941, introduced unipolar precordial leads with the suggestion that, by this method, direct or semi-direct recordings from various points on the epicardial surface were obtained. At first the tracings were believed to reflect electrical activity referable to the underlying portions of myocardium, and were correlated with the terms dextrocardiogram and lævocardiogram introduced by Lewis (1925) after his experimental work on dogs. Later

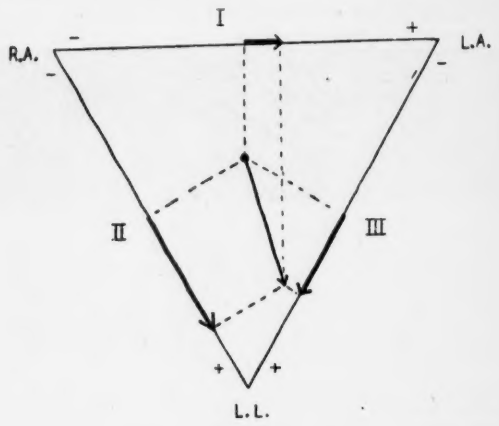


FIGURE I.

Drawing showing the relationship between an instantaneous frontal plane vector (shown by arrow pointing downwards) and its projections on leads I, II and III. Points RA, LA and LL indicate the three limbs on the conventional Einthoven triangle. The + and − signs indicate the polarity of the connexions.

this belief has been modified, and the traces from precordial leads anatomically over the right ventricle are now thought to give a record of electrical activity largely from the right ventricle, but with some interference from the left

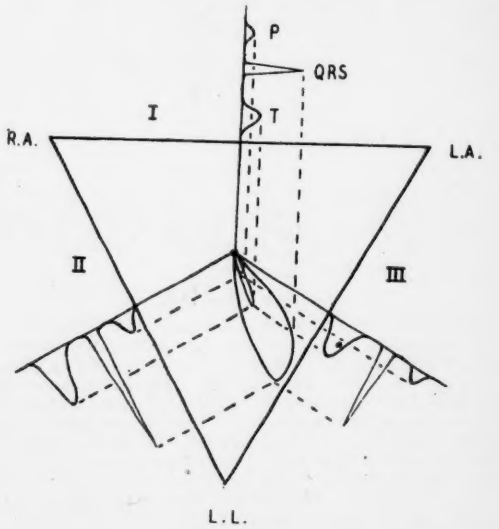
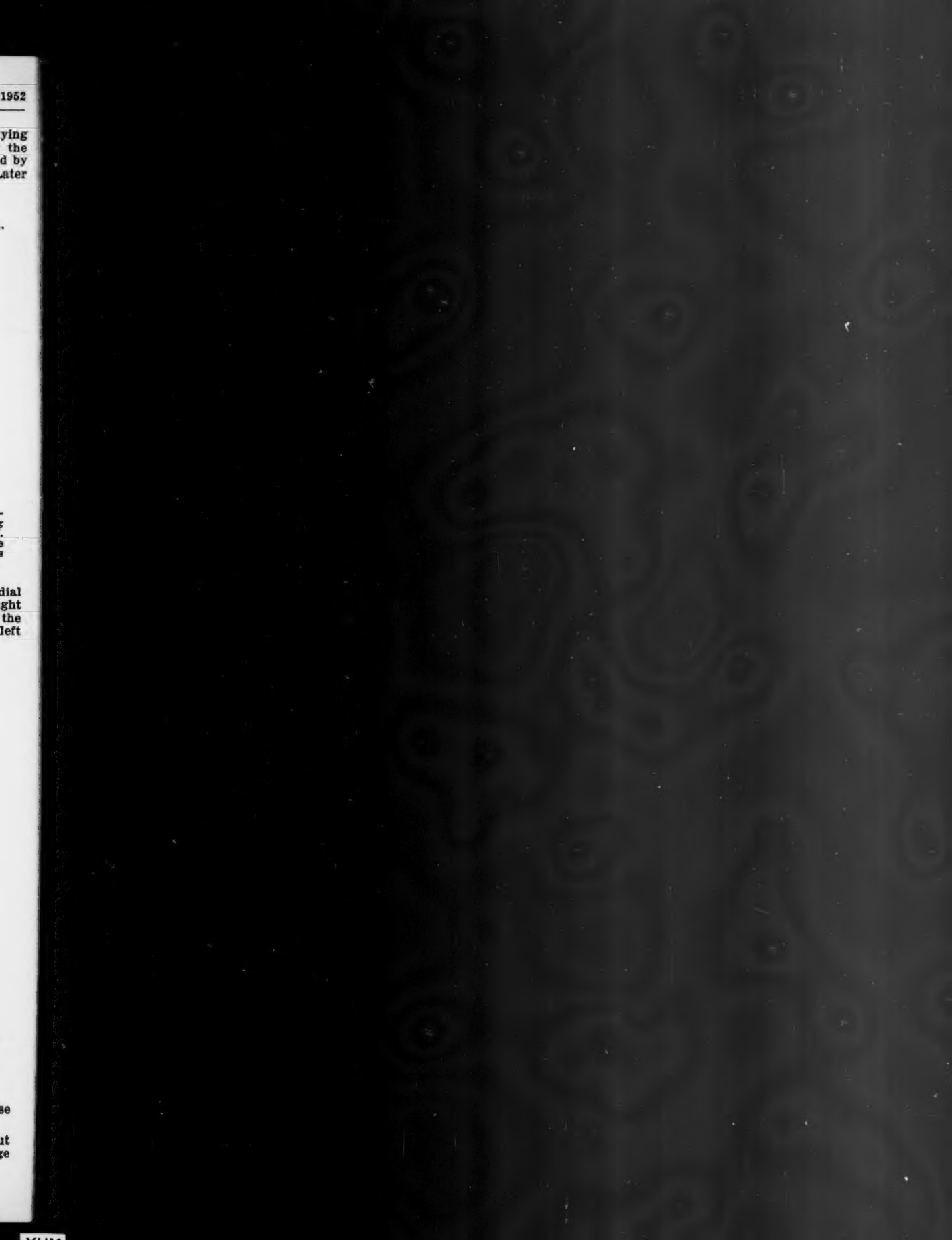


FIGURE II.

Drawing showing the relationship, during one cardiac cycle, between leads I, II and III of the electrocardiogram and the paths inscribed by the free positive ends of the *P*, *QRS* and *T* vectors, as projected on the frontal plane.

ventricle. The leads over the left ventricle give the reverse effects.

However, Duchosal and Sulzer (1949) have pointed out that by extension of the Einthoven hypothesis to envisage



the "manifest" cardiac vector situated in a three-dimensional uniformly conducting medium, the potential changes recorded from the precordium can equally well be accounted for by the component of the "manifest" cardiac vector projected along the axis of that particular recording. They believe that precordial tracings record the horizontal plane component of the "manifest" cardiac vector, with leads V_1 and V_2 in a plane slightly above that of leads V_4 and V_5. The greater the number of precordial tracings recorded, the greater the number of horizontal vector components of the "manifest" cardiac vector studied.

Empirical interpretation of the three bipolar and three unipolar limb leads, together with that of three to nine unipolar precordial leads, is now the usual practice of most physicians. Some investigators remain unsatisfied with the information obtainable from these leads and have added œsophageal, bronchial and intracardial leads, and electrical scanning of the precordium, even to the extent of some 200 tracings from each patient.

If it can be demonstrated that this multiplicity of recordings can be avoided by some all-embracing method, then a simpler technique for studying cardiac electrical activity will have been achieved. It is our purpose in this section to show that, for many purposes, the technique of vector-electrocardiography can replace these multitudinous recordings.

Vectorelectrocardiograms in the frontal plane only were first used clinically by Mann in 1920. As had been suggested by Einthoven in 1913, Mann calculated the loops vectorially from the three standard bipolar leads. In 1936 Schellong used the cathode ray oscilloscope for this purpose. Three-dimensional vectorelectrocardiography was introduced by Sulzer and Duchosal in 1945.

In the present study both graphic and electronic syntheses of the "manifest" cardiac vector have been made, the first by the method of Mann and the latter by means of a cathode ray oscilloscope.

For electronic synthesis of the vector loop the potentials from any pair of leads, at right angles to each other and in one plane of the body, are amplified and applied at right angles to each other across the electron beam of a cathode ray oscilloscope (see Appendix I). The deflections of this beam produce on the fluorescent screen the loops corresponding to the *P*, *QRS* and *T* complexes.

Various electrode placements conforming with these requirements are possible. Thus Wilson and Johnston (1938) first used leads I and V_F to give frontal plane vector loops (Figure III), and later (1947) extended this arrangement to a third dimension by adding a scapular electrode, thereby obtaining a tetrahedral construction. In this method the amplification on lead V_F must be $\sqrt{3}$ times that of lead I to get a true synthesis, and other factors must be used when the scapular electrode is in the circuit.

Scherlis *et alii* (1951) used a cubic construction from which paired leads were selected to obtain the vector-electrocardiogram in the frontal, sagittal and horizontal planes.

Schellong *et alii* (1937), and Duchosal and Sulzer (1949) use two different cuboidal orientations of electrodes. In the method of the latter workers (see Appendix II) the cardiac centre is taken as being beneath the fifth left intercostal space, three centimetres to the left of the mid-sternal line. Electrodes placed on the right shoulder and the right lumbar regions provide a vertical lead, those on the right lumbar and right hypochondriac regions a postero-anterior lead, and those on the right and left lumbar regions a transverse lead. Correct polarity of leads must be used (Figure IV) in connecting the electrodes to the machine.

From the vertical and transverse leads the frontal vector-electrocardiogram is obtained, from the vertical and postero-anterior leads the sagittal vectorelectrocardiogram, and from the postero-anterior and transverse leads the horizontal vectorelectrocardiogram (Figure IV). It will be noted that as the various vectorelectrocardiograms are formed from different combinations of the same three bipolar leads, there should be no discrepancy in the magnitude of any vector component in the different projections.

As Arrighi (1938) had described a triangular set of electrodes in the sagittal plane (see Appendix III), which behaved like Einthoven's frontal triangle, it seemed to us

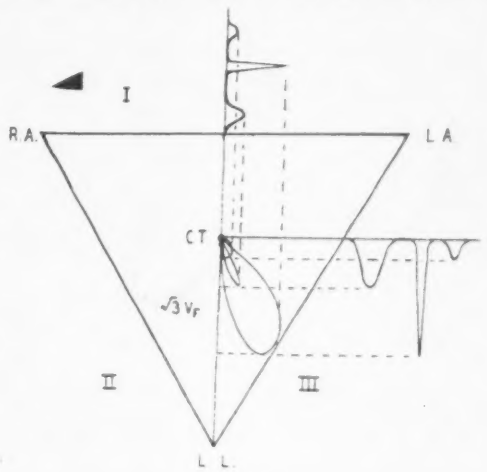


FIGURE III.

Drawing showing the relationship between leads I and V_F of the electrocardiogram in the synthesis of the frontal plane vectorelectrocardiogram.

that these two triangular constructions might be combined to give a synthesis of the "manifest" cardiac vector. The frontal vectorelectrocardiogram was obtained by the use

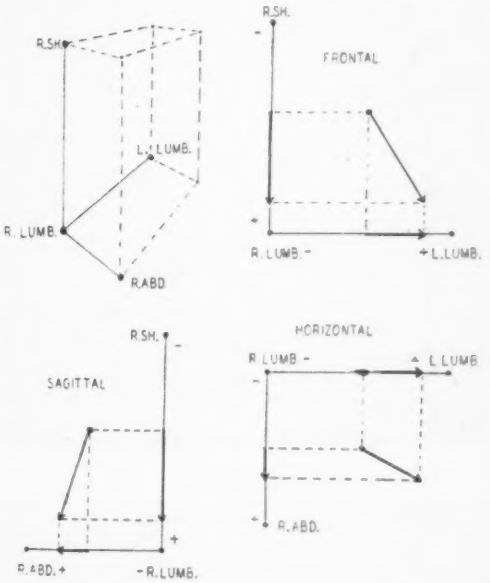


FIGURE IV.

Diagrammatic representation of the electrode placements used for the cuboidal construction of Duchosal and Sulzer. Also depicted are the lead-off points used to synthesize vectorelectrocardiograms in the three planes. "R.SH", right shoulder region; "R.LUMB.", right lumbar region; "L.LUMB.", left lumbar region; "R.ABD.", right hypochondrium.

of leads I and V_F and the sagittal vectorelectrocardiogram by the use of the corresponding leads of the sagittal triangle. From these leads in both planes ordinary electro-

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cardiographic tracings were taken simultaneously on a Grass encephalograph, and the vectorelectrocardiograms were derived by graphical methods. This method was employed in part of the series of normal persons studied.

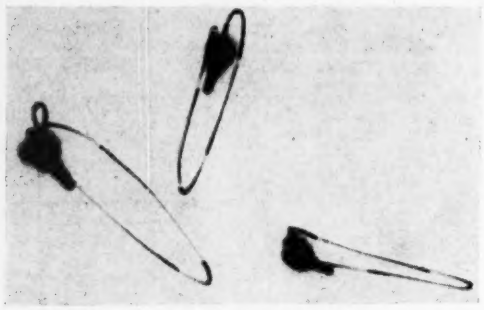

FIGURE V.

Photographs showing the vectorelectrocardiogram obtained from a normal subject. The left one is in the frontal plane, the centre in the sagittal plane and the right in the horizontal plane (see text for orientation).

The larger part of the series was studied by electronic synthesis by means of the technique of Duchosal and Sulzer, with the exception that the vector convention is that of Wilson *et alii* (1938), in which the negative end of the vector is fixed. In the illustrations (Figures V to VIII)

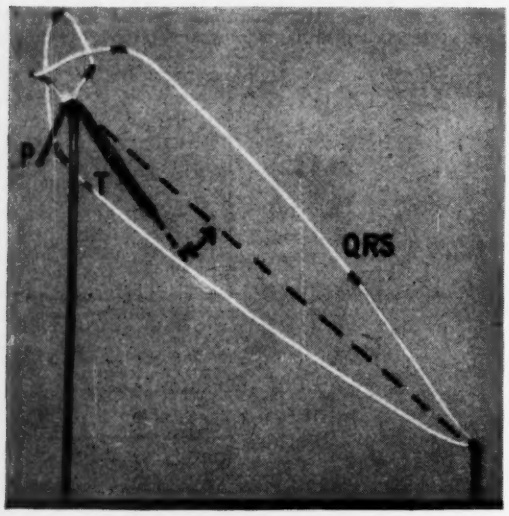

FIGURE VI.

Photograph of a three-dimensional model of a normal vectorelectrocardiogram, showing the long axis of the *QRS* and *T* loops and the *QRS-T* angle between these axes. "*P*", *P* vector loop; "*T*", *T* vector loop. Large white loop is the *QRS* loop, on which the black spots represent time markers 0·01 second apart. Note that the *QRS* loop is of the fourth type described in the text.

the frontal loops are presented as viewed from the front, the sagittal loops as from the left and the horizontal loops as from above. Time relationships are obtained by applying blanking pulses, at known regular intervals, to the electron beam. Vectorelectrocardiograms are taken in either two or three of the frontal, sagittal or horizontal planes. From these two-dimensional tracings, photographically recorded, spatial vectorelectrocardiograms are easily obtained by measurement, and wire loop models are constructed for demonstration purposes (Figure VI).

Demonstration of the Validity of the Method.

Before this method can replace existing methods of electrocardiography, it must be shown that the vector-

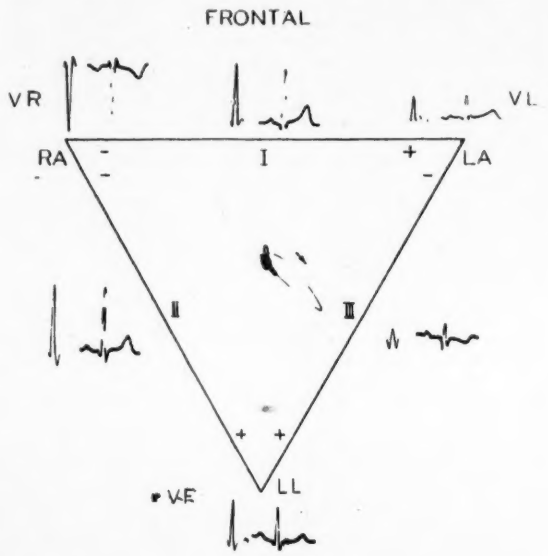

FIGURE VIIA.

A composite picture showing the comparison between observed electrocardiograms and those calculated from the vector loops shown. Shows the comparison between leads I, II, III, V_E, V_L, V_F and the traces calculated from the frontal vectorelectrocardiogram.

electrocardiogram contains all the information usually obtained from bipolar and unipolar leads.

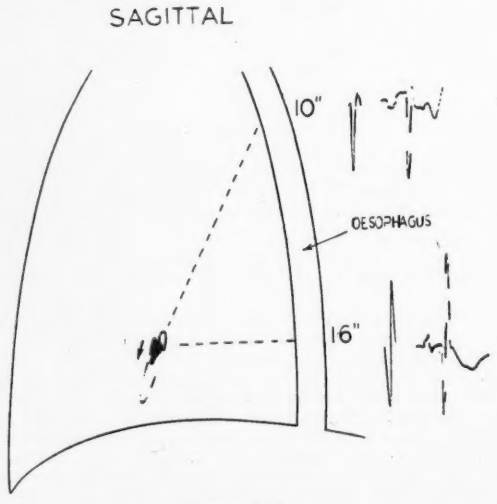

FIGURE VIIB.

A composite picture showing the comparison between observed electrocardiograms and those calculated from the vector loops shown. Shows the comparison between œsophageal leads, taken at 10 inches and 16 inches from the incisor teeth, with the traces calculated from the sagittal vectorelectrocardiogram.

In Figure V are shown the vectorelectrocardiograms from a normal young subject, obtained in frontal, sagittal and horizontal planes.

Figure VIIA is a composite picture of the frontal vectorelectrocardiogram with the zero potential point placed in the centre of the conventional equilateral triangle, the angles of which represent the right arm, the left arm and the left leg. Placed around the triangle are recorded traces of leads I, II, III, V_R, V_L and V_F. Placed beside these records are *QRS* complexes calculated from the frontal vectorelectrocardiogram.

It is noteworthy that for each lead the calculated *QRS* trace corresponds accurately qualitatively with the recorded tracing. Wherever there is a change in the direction of inscription of the calculated trace, a similar alteration in the recorded tracing occurs at the same instant; likewise changes in the rate of inscription are exactly comparable. The ratios *Q:R:S* are the same for calculated and recorded complexes in all leads.

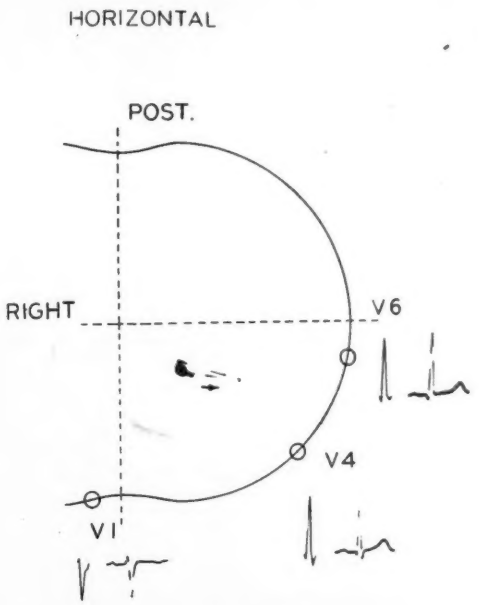

FIGURE VIIc.

A composite picture showing the comparison between observed electrocardiograms and those calculated from the vector loops shown. Shows the comparison between the precordial leads V_1, V_4 and V_6 with the traces calculated from the horizontal vectorelectrocardiogram.

Because of computational difficulties we have not attempted to make a quantitative comparison of voltage levels of the calculated and recorded leads. No calculation of *P* waves has been attempted, as the *P* loops of our records are too small for analysis. Similarly no analysis of the *T* loops has been made, but it is clear that in amplitude and general orientation the T waves obey the same relationship as the *QRS* deflections.

Figure VIIc is a composite diagram showing the horizontal vectorelectrocardiogram placed in relationship with calculated and recorded unipolar precordial electrocardiograms for leads V_1, V_4 and V_6. Once more the qualitative relationship between *QRS* complexes is shown.

Figure VIIB is a composite diagram showing the sagittal vectorelectrocardiogram placed in relationship with œsophageal recordings at 10 and 16 inches from the lower incisor teeth. The same relationships are again apparent. The records from this patient show that, to a close approximation, the spatial vectorelectrocardiogram gives an accurate condensation of a comprehensive series of leads, and in numerous other reconstructions we have found no real discrepancies between predicted and observed recordings.

Several systems of electrode placement for vectorelectrocardiography have been mentioned, and some discussion of their merits and difficulties is necessary.

The electrode placements in the sagittal triangle are relatively much closer to the heart than are those of the frontal triangle, and minor errors in placement of electrodes result in fairly pronounced alteration in the amplitude of deflection along one or other axis. This leads to corresponding alteration in the axes and contours of the vectorelectrocardiograms.

We have found discrepancies of up to 30% in amplitude of the vertical component of the vector when determined from the two triangles. Though the vectorelectrocardiograms obtained by this method, whether by calculation or electronically, permit qualitative interpretation, this interpretation appears less accurate than that of vectorelectrocardiograms obtained from the cuboidal arrangement of leads (compare Figures IXA and B).

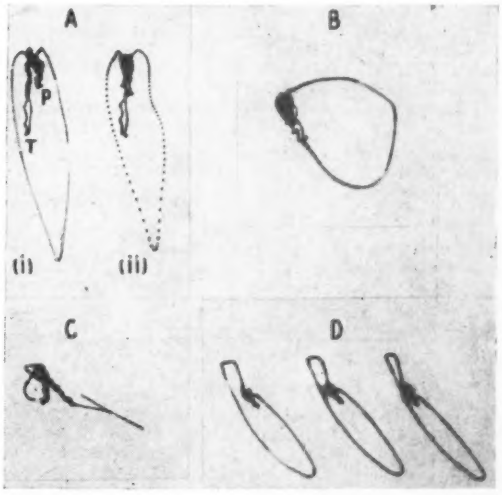

FIGURE VIII.

Normal vector loops in frontal plane. A: from a vertical heart, showing the varying speed of inscription indicated by the distance between time markers (i) 0·01 second apart, (ii) 0·001 second apart. B: from a horizontal heart showing a smooth *QRS* contour. C: showing both initial and final deflections of the *QRS* in a direction opposite to that of its long axis. D: showing variation produced by respiratory movement.

The cubic or cuboidal constructions have several advantages. Only four instead of six electrode placements are needed. All the electrodes are placed at a similar and considerable distance from the cardiac centre, and although the distance between electrodes used for the bipolar lead varies from patient to patient, adjustment of amplification for each has been found empirically to be unnecessary (Duchosal and Sulzer, 1949). Calculated electrode placement is found to be unnecessary once one becomes acquainted with the usual placement sites for different body builds.

The Normal Vectorelectrocardiogram: Analysis of QRS and T Loops.

Although several descriptions of the normal vectorelectrocardiograms have been given (Sulzer and Duchosal, 1946; Grant, 1950; Grishman *et alii*, 1951), the number of observations in the series reported by these observers is small. In the present survey 104 individuals have been examined, and in general the results confirm the findings of the authors mentioned, but indicate considerable variation in the normal pattern. However, normal limits appear to be well defined.

All the individuals selected were free from any evidence of cardio-vascular disease. Their ages were between five and seventy-five years. There were 51 females and 53 males. The vectorelectrocardiograms of 36 of the young women were computed by graphic methods, and as the results obtained agreed closely with those of the electronic method (see Figures IXA and B), they have been considered together.

In the normal subject, the vectorelectrocardiogram, though varying in details of pattern, possesses certain characteristics which are constant within a fairly narrow range. These are as follows: (i) the duration of the *QRS* vector loop; (ii) the direction of the long axis of the *QRS* vector loop; (iii) the spatial angle between the long axis of the *QRS* and *T* vector loops; (iv) a common point of origin and termination for both *QRS* and *T* loops.

The Duration of the QRS Vector Loop.

The duration of the *QRS* vector loop is from 0·6 to 0·8 second, which corresponds with the duration of the *QRS* complex. However, there is considerable variation in the rate of inscription of different parts of the loop, which is indicated quantitatively by the distance between successive blanking pulses. At first there is a short slow inscription, followed by the larger portion of the loop which is inscribed rapidly. The terminal portion of the loop, prior to the return to the zero point, is again inscribed slowly. In the normal vectorelectrocardiogram these varying speeds of inscription merge into one another, there being no sudden alteration in speed (see Figure VIIIA).

Direction of the Long Axis of the QRS Vector Loop.

The long axis of the *QRS* vector loop is the line joining the origin to the furthest point of the spatial loop. In any one plane the point on the loop which is furthest from the origin is easily determined, but care must be exercised to see that corresponding points are taken in the loops of different planes. Occasionally it is not obvious which points correspond, and then either reliance must be placed on the time markers, if simultaneous tracings are made, or the spatial model must be constructed.

The direction of the long axis can be expressed as an angle on a scale of coordinates, and Figure IX shows the coordinates used in this study.

The ranges of angles observed in these cases are as follows: (*a*) frontal plane, 10° to 90°; (*b*) sagittal plane, 60° to 130°; (*c*) horizontal plane, −30° to +30°.

The diagrams of Figure IX show the frequency distribution of the various angles in each plane, the results in Figure IXA being obtained by graphic construction. It is to be noted that the scatter of the latter results is slightly greater than is obtained with electronic synthesis, and this

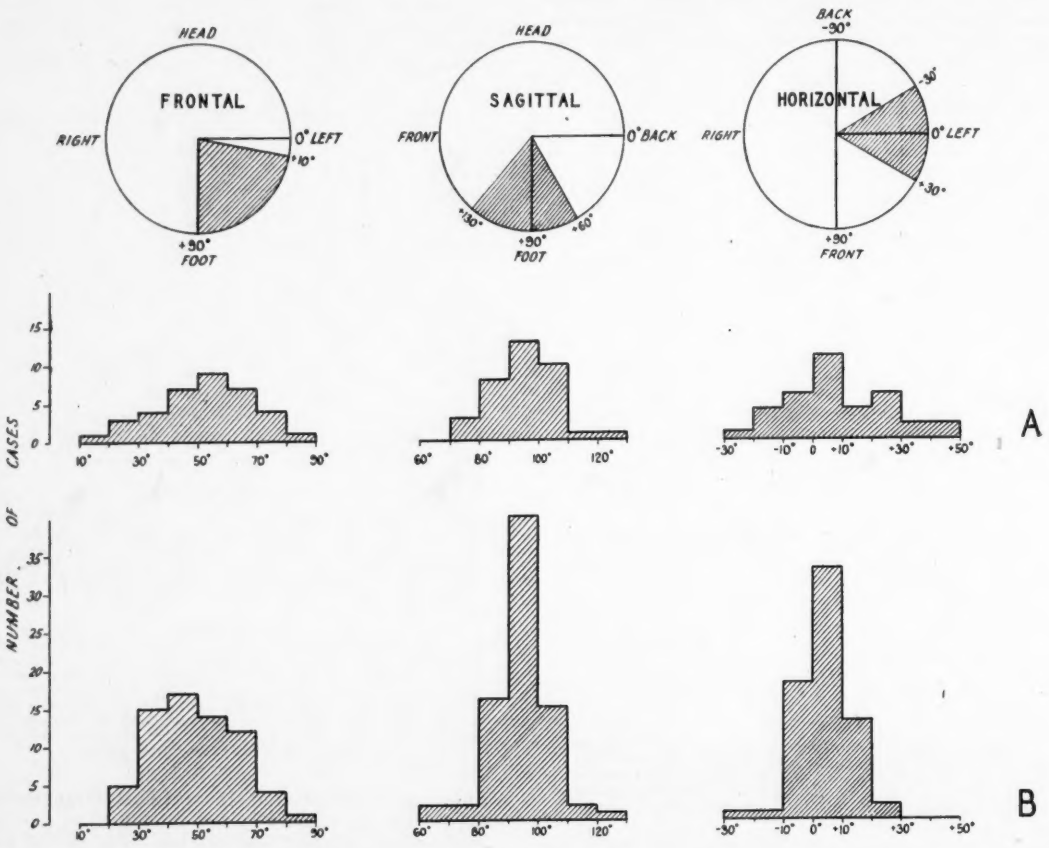

FIGURE IX.

Diagram illustrating the coordinate system used in stating the angles of the axes of the *QRS* vector loop. Shaded areas of circles indicate the zones in which these axes normally lie. The histograms (A) show the frequency distribution of the *QRS* axis angles in various planes. These were constructed graphically from conventional electrocardiograms. The histograms (B) indicate the frequency of distribution of the *QRS* axis angles in various planes from the series in which instrumental synthesis was used.

is thought to be an expression of the more accurate synthesis made by the machine.

The long axis of the loop for the normal subject, obtained by means of the electrode placements described, points to the left, downwards and either slightly backwards or forwards.

The Spatial Angle Between the Long Axes of the QRS and T Vector Loops.

Grant (1950), from a study of a large series of unipolar precordial leads, pointed out that the most significant factor in the interpretation of *T* wave changes in electrocardiograms is the spatial angle between the long axes of the *QRS* and the *T* loops (see Figure VI), and that this is less than 30° in normal subjects below the age of fifty years. This angle can be obtained from the vectorelectrocardiograms by calculation and often approximated by inspection.

Calculation of this angle is somewhat tedious, but inspection of the loops in most cases indicates whether the *QRS–T* angle is within the limits of normality. For technical reasons accurate calculation of the *QRS–T* angle was possible in only 56 cases of the series, and in these it lay between 0° and 30°. Table I shows the frequency distribution of the various angles. Subdivision of the cases into age groups shows no evidence that, as Grant has suggested, the *QRS–T* angle increases with the age of the subject.

TABLE I.
QRS-T Angle.

Age. (Years.)	Number of Subjects.						
	0° to 4°.	5° to 9°.	10° to 14°.	15° to 19°.	20° to 24°.	25° to 30°.	Total.
0 to 15	6	4	4	2	4	2	22
16 to 40	6	6	5	5	2	3	27
Over 40	1	3	—	2	—	1	7
All ages	13	13	9	9	6	6	56

Point of Origin of QRS and T Vector Loops.

In the normal subject both the *QRS* and *T* vector loops commence and terminate at the same spot, and between the finish of the inscription of the *QRS* loop and the commencement of the *T* loop the tracing is stationary at the origin. This period corresponds to the isoelectric *S–T* segment of the electrocardiogram.

Two other characteristics of the *QRS* vector loop which are less constant than the foregoing require mention; they are the direction of inscription and the contour of the loop.

Direction of Inscription of the QRS Vector Loop.

In these normal subjects the direction of inscription of the *QRS* vector loop was either clockwise or anti-clockwise in the frontal plane, but was always anti-clockwise in the sagittal and horizontal planes. The direction of inscription was recorded in 64 cases, and in the frontal plane 28 inscriptions were written clockwise and 36 anti-clockwise.

The Contour of the QRS Vector Loop.

The shape of the *QRS* vector loop varies from individual to individual, and may be broad and rather rounded or narrow and elongated. In general the narrow elongated form (see Figure VIIIA) is found in individuals having a vertical heart in a narrow chest, and the broad (see Figure VIIIB) in those of heavier build with hearts more horizontal in position.

As the spatial vector loop is not inscribed on a flat surface, but one which undulates, its projection on to any given two-dimensional plane may give a figure-of-eight appearance.

In this series four basic types of loop have been noted, as follows. (i) The simplest form of vector loop seen has a smooth contour and its origin at one end (see Figure VIIIB). (ii) In some subjects there is an initial small portion of the loop inscribed in a direction opposite to the main portion of the loop. (iii) In other subjects there is a terminal portion similarly inscribed away from the main loop position (see Figure VIIID). (iv) Occasionally both the initial and terminal deflections opposite to the major part of the loop are present (see Figures VI and VIIIA and VIIIC).

In many persons, in one or other plane, a pronounced change in the shape of the vector loops occurs with respiratory movement of the chest (see Figure VIIID). In general this is due to the changing projection of the spatial loop on to the observed plane, and is brought about by rotation of the heart with respiration. Frequently there is also some alteration of the direction of the long axis of both *QRS* and *T* loops. These changes are most easily discerned by continuously observing the tracings on the fluorescent screen. Similarly in many subjects changes in posture will alter the position of the heart relative to the chest walls and likewise alter the projection of the vector loop.

In children these respiratory and postural changes in the vector loop projections are often pronounced. At times there is considerable movement of the origin even during one cardiac cycle. This phenomenon corresponds to the wandering base line seen in electrocardiograms of children. Although in the presence of these movements calculation of some of the constants of the vectorelectrocardiogram—for example, the spatial *QRS–T* angle—is impossible, it is nevertheless possible to say by inspection whether or not the vectorelectrocardiogram is within normal limits.

Commentary.

It is seen from this study that vectorelectrocardiography has certain definite advantages over conventional electrocardiography. For although vectorelectrocardiograms contain the same information as can be obtained from traditional electrocardiograms, this information is presented to the observer in two traces, so that the need to memorize the normal variations of a large number of tracings is obviated.

Further, as the heart's "manifest" electrical activity is studied in three dimensions, variations in tracings due to positional change of the heart in the thorax are readily recognized.

Also, as the electrode placements used are at a considerable distance from the heart, minor errors in siting do not appreciably alter the tracings recorded. This is in great contrast to the necessity for accurate placement of precordial electrodes for electrocardiography.

It is a simple matter to incorporate in the vectorelectrocardiograph a switch so that cardiac events may be portrayed against a time base. This enables disturbances in rhythm to be elucidated with greater facility than from serial vectorelectrocardiograms.

In conclusion, it may be stated that vectorelectrocardiography is at present a research tool which shows promise of simplifying the recording and interpretation of the heart's electrical activity.

Summary.

The technique of vectorelectrocardiography is discussed and described in detail.

The features of the vectorelectrocardiogram in a series of 104 normal subjects are described.

Acknowledgements.

We wish to express our appreciation and thanks to the many colleagues and assistants who have made possible this investigation. In particular our thanks are due to Mr. D. Dewhurst, Physiology Department, University of

Melbourne, and Mr. A. L. Weller, of the Clinical Research Unit, Alfred Hospital, who designed and constructed the vectorelectrocardiograph.

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Appendix I: The Vectorelectrocardiograph.

From the description of the technique it is clear that the vectorelectrocardiograph consists of a two-channel electrocardiograph in which each channel is fed to one pair of the deflecting plates of the cathode ray oscilliograph.

In this investigation each channel consists of a three-stage R-C coupled valve amplifier, of which the first two stages are battery driven. The maximum overall amplification obtainable gives a spot deflection on the fluorescent screen of greater than 12 centimetres for one millivolt input signal. Generally it was found that a standardization of six centimetres per one millivolt input signal was adequate.

When a cuboidal electrode framework is used, equal amplification of the signals by both channels is necessary. This necessary balance is obtained by introducing a 50 cycle alternating current signal simultaneously into both amplifiers and adjusting their gain until the resulting spot deflection on the screen is a line at 45° to the horizontal.

The frequency response of the apparatus, including the shielded leads from the patient, is good up to 100 cycles per second, but beyond this limit the response falls rapidly and is ineffectual above one kilocycle per second. However, in many patients it is found necessary to suppress higher frequencies to avoid disturbance from muscle action currents. Most of the normal vectorelectrocardiograms of the present series were taken with the time constant of the apparatus at about 0·5 second. Although this would be too low for accurate recording of many abnormal conditions, it has produced no noticeable distortion in the normal records.

A blanking pulse introduced into the circuit every 0·01 or 0·001 second provides a time marker on the vector loops. Appropriate lead switching and the incorporation of a sweep circuit enable traditional electrocardiograms to be taken for comparison with vector loops.

As the records on the fluorescent screen are photographed, a fixed-focus stationary film camera is permanently mounted over a cathode ray tube with a blue non-persistent screen. In parallel with this tube is another cathode ray tube with a persistent screen, which is available for continuous monitoring observation.

Provision is made in the apparatus for two additional channels to feed a second cathode ray oscilloscope. It will then be possible to photograph the vector loops in two planes simultaneously and possibly reduce the whole procedure of vector electrocardiography to the taking of one photograph.

Appendix II: Placement of Electrodes for the Construction of Duchosal and Sulzer.

The distance of the cardiac centre from the right side of the chest in the horizontal plane passing through the fifth intercostal space is measured, and two horizontal planes this distance above and below the cardiac centre are then obtained. The diameter (D) of the trunk at the level of the cardiac centre having been noted, one electrode is then placed in the upper plane posteriorly at a distance D/3 to the right of the mid-line. This usually lies on the spinous process of the right scapula. Three electrodes are placed in the lower plane, D/3 from the mid-line, posteriorly one to the left and one to the right, and anteriorly one on the right. These electrodes usually lie over the left and right lumbar regions below the twelfth rib, and in the right hypochondrium.

Appendix III: Placement of Electrodes for the Sagittal Triangle Construction of Arrighi.

The sagittal triangle is constructed by placing electrodes three centimetres to the left of the mid-line, on the chin, on the back at the level of the seventh thorac spine, and on the abdomen midway between the umbilicus and the *symphysis pubis*. The lead chin-back corresponds to lead I and the lead abdomen-central terminal corresponds to lead V_F.

A SURVEY OF 681 CHILDREN AWAITING TONSILLECTOMY AND THE INDICATIONS FOR OPERATION IN CHILDHOOD.

By David L. Dey,

The Institute of Child Health, University of Sydney, and the Royal Alexandra Hospital for Children.

As a result of the suspension of routine tonsil and adenoid operations during the recent poliomyelitis epidemic, some 1415 children had been held on the waiting list of the Royal Alexandra Hospital for Children for an average period of eighteen months. Except for a few children whose admission to hospital had been arranged on the authority of a letter from their own practitioner, these patients had been referred for operation from the out-patient department of this hospital. The majority of these recommendations had been made by members of the honorary surgical staff, and the others by members of the ear, nose and throat department. These children, therefore had all been regarded by an experienced observer as requiring operation. It was thought that a reassessment would provide much valuable evidence in the local consideration of the problem of tonsillectomy and also some information as to the natural history of upper respiratory tract infections.

Method.

A request to present for reexamination was sent to the parent or guardian of each of the 1415 children. In response to this request a total of 681 children reported for examination. The age distribution of these children was as shown in Table I.

A careful history was taken, with special inquiry into symptoms referable to the ear, nose and throat. An assessment of the general physical state of the child was then made, the fauces, oral cavity and pharynx were examined, and the face, scalp and other surface areas were inspected. Finally the cervical lymph nodes were palpated, including those of the posterior triangle, and the findings were recorded. The height and weight of the child were also measured and recorded.

XUM

In an attempt to estimate the state of the children who were not presented for examination, after the original request a further letter, together with a *questionnaire* and a stamped and addressed envelope, was sent to 100 of their parents, picked out at random. The results were as follows: (i) 40 children had undergone operation elsewhere; (ii) 11 children were so well that the parents considered operation unnecessary; (iii) fear of the poliomyelitis epidemic had prevented operation on four children; (iv) eight letters were returned unclaimed; (v) operation had been deferred for domestic and administrative reasons in seven cases; (vi) no reply was received in 30 cases; total, 100.

RESULTS.

In the case of each child a decision was made on the basis of the following principles: (i) that patients whose symptoms were purely those of adenoidal enlargement —obstruction of the post-nasal space or of the Eustachian tubes—should be regarded as constituting a separate problem, and not requiring tonsillectomy; (ii) that the appearance of the tonsils and the size of the cervical lymph nodes were of minor importance, and were not to be taken into account if there had been an attack of tonsillitis in the past two months; (iii) that a careful history and an analysis of the symptoms should form the chief guide in arriving at a decision; (iv) that an operation for removal of tonsils and adenoids should almost never be undertaken before the age of four years, the only exceptions to this being the rare cases of gross obstruction from enlarged tonsils or adenoids or of gross infection not controlled by antibiotics. In such urgent cases in children aged under four years certain precautions are necessary (see later).

TABLE I.

Age. (Years.)	Number of Children.	Age. (Years.)	Number of Children.
2	3	8	74
3	32	9	52
4	98	10	30
5	126	11	27
6	110	12	20
7	102	13	7

The following were regarded as definite indications for tonsillectomy. (*a*) A clear-cut history of recurrent attacks of tonsillitis, with at least three or four attacks each year, extending over at least two winters, such attacks being associated with pyrexia, or at least being severe enough to put the child to bed or prevent his attendance at school. (*b*) Quinsy. (*c*) Upper respiratory tract infections followed frequently by attacks of bronchitis and not occurring independently of the colds or sore throats. (The adenoids are of chief importance in this group.) (*d*) Gross enlargement of tonsils with mechanical obstruction—a rare condition. (*e*) Tuberculous cervical adenitis—this is a special problem outside the scope of this survey.

The 681 children were grouped into three main categories, as follows: Group I: those requiring tonsillectomy, 331; Group II: those having symptoms referable only to the adenoids, 98; Group III: those no longer requiring operation, 252. Group III was further subdivided as follows: (*a*) children without symptoms, 78; (*b*) children who had a history of only one attack of tonsillitis, none since the first recommendation, 38; (*c*) children who had symptoms for a short period at and about the time of recommendation, none since, 47; (*d*) children with symptoms regarded as too mild to warrant operation, 49; (*e*) children with symptoms attributed to an allergic state, 25; (*f*) children with bronchitis not apparently connected with upper respiratory tract infections, 15; total, 252.

Group III.

Group III is probably of the greatest interest, and at the same time the classification requires some amplification.

Sub-group III (a).

The first sub-group consisted of children without symptoms. The mother in these cases stated that the child "never missed school". In at least 33 cases a letter from the School Medical Service pointing out that the child needed advice was the motive factor, and apparently in most of the others the local medical practitioner or a neighbour or relative had instigated presentation. The factor influencing the subsequent recommendation for operation was apparently the result of the physical examination, and certain comments on the physical signs are necessary.

It is of considerable importance that the appearances of the tonsils, and the size of the draining lymph nodes, did not obviously vary between those children regarded as requiring an operation and the remainder. Almost without exception, the children examined had moderately enlarged tonsils, often with bands of scar tissue on the surface and obvious crypts. This appears to be a usual finding in children in this age group, except during infective episodes. The hypertrophy and œdema of such an episode may take a month or two to subside, and therefore physical examination alone is of no value as an operative indication during that time.

It was exceptional for the draining lymph nodes to be impalpable. Whilst it was by no means invariable, however, those children without any symptoms had slightly smaller nodes generally than those of the others. From this survey it would seem that some degree of persistent enlargement of the tonsillar nodes is a usual finding in young children, and in this respect two points should be remembered: (i) that the "tonsillar glands" drain not only the tonsils but a wide field including the mouth (teeth), ear and scalp. Therefore, a search should be made for other foci in this field before such enlargement is regarded as tonsillar—it may even be part of a generalized lymphadenopathy; (ii) that the normal response of a lymph node to any adequate stimulus, including infection, is by hypertrophy—this is a normal defence mechanism and is not in itself a reason for operation.

A further similar fallacious "physical finding" that can be considered here is the degree of "fatness" or "thinness" of the child. In this regard the "growth periods" must be kept constantly in mind. Normally the child "springs up" in the five-year to seven-year period, losing his baby-fat, and frequently appearing comparatively thin and weedy. This is also a period of change in the child's life, which may determine a good deal of mental stress and consequent ill-humour. A tonsillectomy performed during this period gets all the credit for the subsequent return to an attractive plumpness and serenity.

Sub-group III (b).

The second sub-group consisted of children who had a history of one attack of tonsillitis only; this heading is self-explanatory. Once again the reason for recommendation has been the appearance of the tonsils and the size of the lymph nodes, and if the attack of tonsillitis had occurred shortly before the child was examined these may have been striking. The size of the group stresses the danger of recommending operation for a child having or recovering from its first attack of tonsillitis.

Sub-group III (c).

The third sub-group consisted of children with short-lived symptoms. It is of interest in that it gives a lead to the period for which symptoms may exist and then disappear. This period appears to be most commonly of from twelve to twenty-four months, often including two winters.

Sub-group III (d).

The fourth sub-group consists of children with symptoms too mild to warrant operation; it includes those children who in their mother's opinion had more than the usual quota of colds or other respiratory symptoms. However, on close inquiry it was found that upper respiratory tract

infections were not the cause of any significant loss of school time, or that an attack of tonsillitis occurred perhaps once in twelve or eighteen months.

Sub-group III (e).

The fifth sub-group—the "allergic group"—comprises those children with a rather indefinite story of respiratory infection, who suffered from asthma, hives or other allergic phenomena, or who had a strongly suggestive family history—particularly when their symptoms suggested a seasonal incidence. The frequency with which asthma in such children is said to date from an operation on the nose and throat, and the poor results of operation anyway, both compel caution. In other words, operation should be carried out only on the clearest possible indications, when it is quite certain that the signs and symptoms are not a result of the allergic state, but are produced by infection.

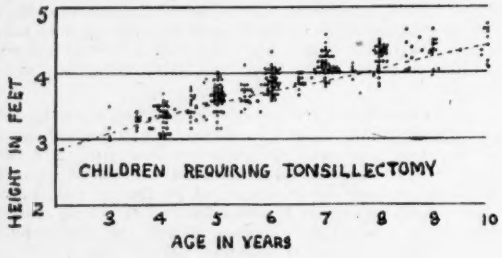

Figure I.

Sub-group III (f).

The sixth sub-group is the "bronchitic group". In those cases in which the complaint was recurrent bronchitis, the nose and throat were not regarded as of importance unless the bronchitis was preceded by attacks of upper respiratory tract infection. In this regard the recent statement of H. B. Harwood (1951) is of considerable importance. In a paper on "Pre-Bronchiectasis", which was read before a meeting of the Oto-Laryngological Society of Australia, and

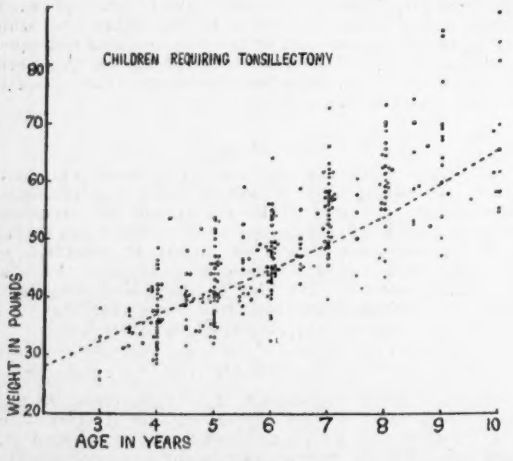

Figure II.

in which he discussed the treatment of children with chronic cough, appears the following:

> Throughout both groups (comprising 50 cases), all but five patients had had tonsillectomy performed as treatment before coming up for consultation. This operation was usually performed around the age of four years, but after operation the patients showed no pronounced or only very temporary improvement.

The impression was gained in all these cases in Group III that the local appearance of the tonsils and the size of the regional lymph nodes had been an important factor in the original recommendation.

Group II.

Among the group with nasal or aural symptoms only, the incidence of a true "adenoidal facies" was extremely low, not more than four or five examples being seen. It must be a rare finding in younger children. Many had a broad nose. In this group the symptoms were solely those of Eustachian tube blockage—repeated earache, deafness, *otitis media, et cetera*—or of actual nasal obstruction, and possibly sinusitis. It was thought to be unreasonable to expect these mechanical factors to be relieved by removal of the tonsils, which lie at some little distance from the various channels named. As is well shown in other parts of the body, chronic infection is a consequence of inter-

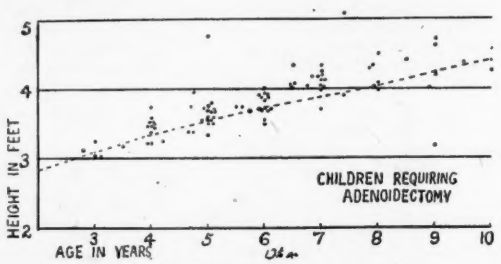

Figure III.

ference with drainage, rather than the factor causing such interference.

It is of interest that six children were examined who had suffered an isolated attack of *otitis media* at least two years before—one with actual mastoiditis. As there had not been a recurrence, one cannot help wondering whether a first attack of *otitis media* in a child who has not previously presented symptoms of nasal or Eustachian tube blockage necessitates adenoidectomy without further question.

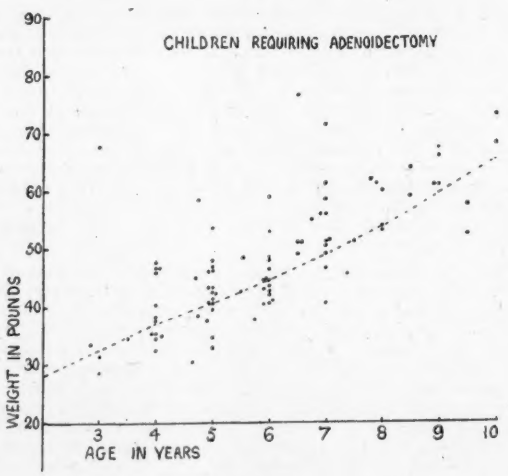

Figure IV.

Group I.

The children regarded as requiring tonsillectomy were subjected to most scrutiny. From the history given by the mother they were regarded as having suffered from repeated attacks of acute tonsillitis.

These children did not present any clinically recognizable feature to suggest that these attacks *per se* had affected their health; with a few exceptions they were well up to the standard height and weight for their age.

This point is clearly shown in the scatter graphs (Figures I, II, III and IV). The mass of the children lies above the line representing the accepted normal in each graph, and the spread is well within the limits of normal variation. One child only (Figure III) shows any significant variation below the accepted normal, and in this case there was present a constant cough with sputum which strongly suggested bronchiectasis.

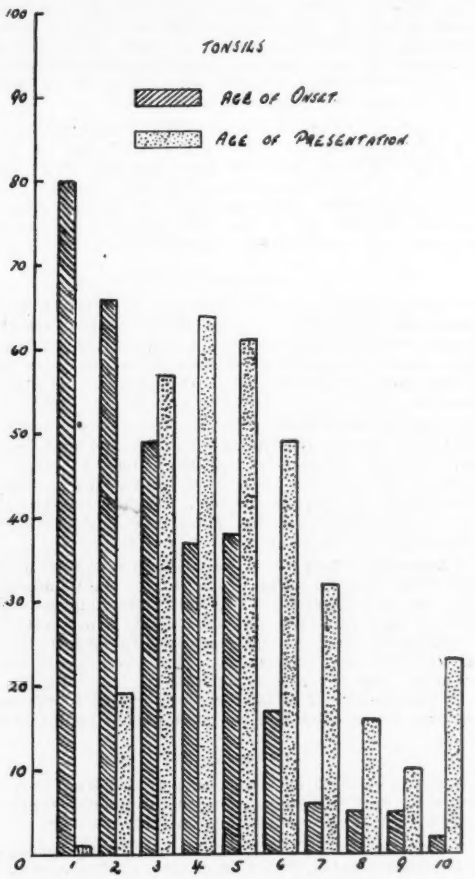

FIGURE V.

After inquiry into the story of those children suffering from anorexia, it was thought that vagaries of appetite are so common, and their relation to a definite history of tonsillitis is so vague, that other factors appear of equal importance in determining this. There is no doubt that when the tonsils and adenoids have been removed on adequate indications there is often a striking improvement in appetite. On the other hand, anorexia cannot be regarded as an indication in itself.

Mortality.

Certain other aspects of the problem appeared of importance, and some inquiry was made into these, an attempt being made first to assess the risks of operation. In the five-year period 1945 to 1950, some 18,912 children were submitted to the operations of tonsillectomy and adenoidectomy in this hospital. Of these children six died within forty-eight hours of operation, and it is immediately obvious that six deaths in 18,912 cases—one death per 3152 cases—represents an appreciable mortality. Further, this is in an institution properly equipped and with a skilled surgical and resident staff. The causes of death were as follows: (i) patient aged two years eight months, septicæmia within twenty-four hours of operation; (ii) patient aged seven

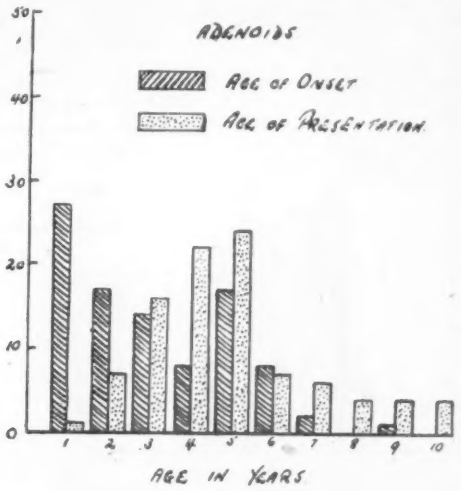

FIGURE VI.

months, pneumonia within forty-eight hours of adenoidectomy only; (iii) patient aged two years nine months, post-operative hæmorrhage in twelve hours; (iv) patient aged four years nine months, collapse under anæsthesia (cardiac); (v) patient aged one year, bronchopneumonia and possible septicæmia within forty-eight hours after adenoidectomy; (vi) patient aged three years six months, collapse under anæsthesia (cardiac).

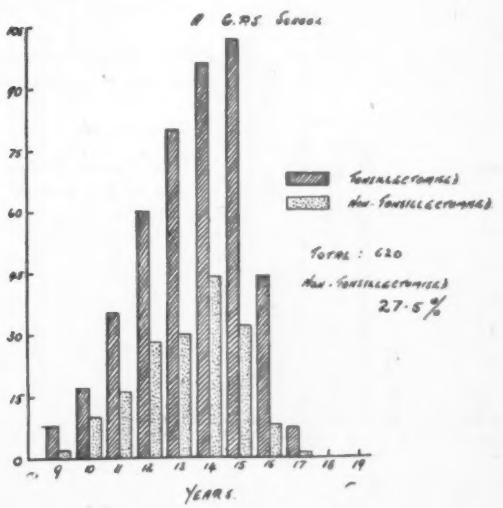

FIGURE VII.

The average age must be considered another factor making operation before the age of four years a procedure to be undertaken with some caution, and a penicillin "cover" would appear a reasonable precaution in this earlier age group in view of the part played by infection.

Morbidity.

The morbidity rate following operation is difficult to assess, owing to imperfect records; but some 1% of children had primary hæmorrhage of sufficient degree to require active measures for its arrest—approximately one in five of these needed blood transfusion. Besides the factor of hæmorrhage, respiratory complications are not an unimportant feature, and most authors are of the opinion that lung abscess or bronchiectasis is an occasional complication of an operation on the upper respiratory passages.

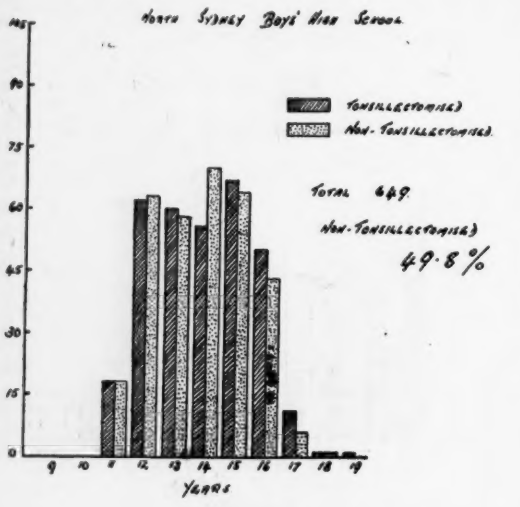

FIGURE VIII.

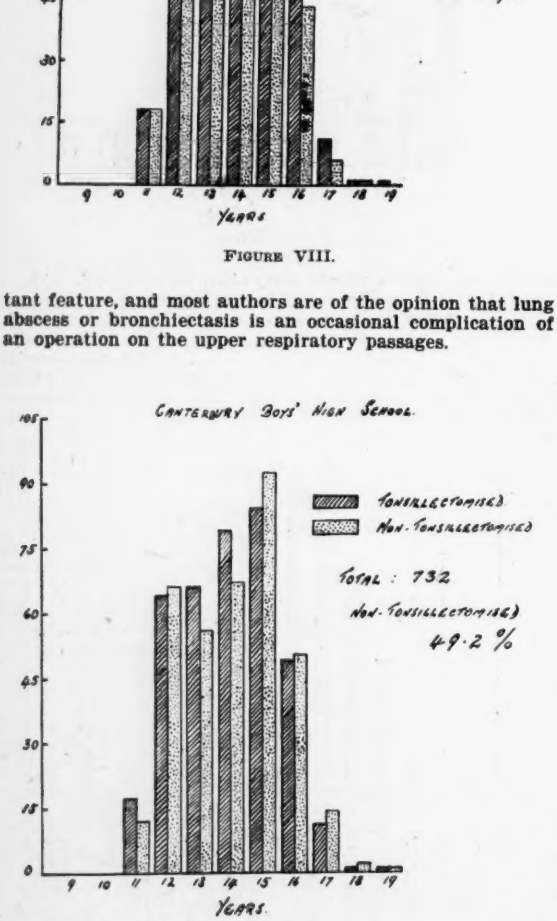

FIGURE IX.

Age of Onset.

The two graphs (Figures V and VI) showing the age of onset of symptoms compared with the age of first presentation at the out-patient department are of interest. The peak of the onset of symptoms from the mothers' histories falls in the first year of life, and the steady decline from this point, with a surprisingly small interruption at five years (school age), is not in accordance with the conventional view.

The age of presentation for examination emphasizes the general tendency to refer these children at an early age.

Parental Infection.

The question of parental infection in ætiology was considered, inquiry being made for recurrent sore throats, sinus trouble or "catarrh" in any adult having intimate contact with the child. The condition of older brothers and sisters was ignored, unless a gap of more than a year or two in age existed. The results were inconclusive: (*a*) children with symptoms beginning in the first two years, parental infection 45%; (*b*) children whose symptoms began after the first two years, parental infection 42%; (*c*) children not requiring tonsillectomy, parental infection 36%. The differences are not thought to be sufficiently striking for any conclusions to be drawn.

The apparent effect of the family's economic status is shown in the graphs in Figures VII, VIII and IX. At a Great Public School 72·5% of boys had had their tonsils removed; at a boys' high school in a neighbouring district 50·2% had had their tonsils removed; at a boys' high school in another district 50·8% had had their tonsils removed. These figures are statistically significant.

Discussion.

Whilst the foregoing contains much suggestive data, it is realized that it contains no proof of the correctness of the principles and indications for operation given earlier. A further examination of the children in two or three years' time may help to support them. It is hoped that this will be possible.

The survey does underline the danger of using the appearances of the tonsils and the size of the regional lymph nodes as indications for operation. I believe that the best guide to the adequacy of indications as supplied by the history is to ask oneself: "Would I agree to an operation if these were my symptoms and if this was my throat?"

The figures given of the actual incidence of the operation clearly show the very large proportion of the population at present being subjected to it, and some popular beliefs about the age of onset of respiratory symptoms, their relationship to entrance into school life and their effect upon the child are questioned. There is support for the observation that the rate of operation rises with the rise in economic status. The dangers of operation in the earlier age groups are shown, and the part played by infection is stressed.

Summary.

1. A group of children whose ages varied from two years to thirteen years had been referred for tonsillectomy with adenoidectomy, or for adenoidectomy alone.

2. A review of these children, after a waiting period of at least eighteen months, based on clinical evidence, suggested that over one-third no longer required operation.

3. Certain features of the indications for these operations are considered.

Acknowledgements.

My thanks are due to Professor Lorimer Dods for his help and encouragement in this survey; to Dr. F. W. Clements for his advice and criticism of the manuscript; to Dr. H. O. Lancaster for his consideration of the statistical features; to the School Medical Service and particularly Dr. K. Myers for their help in providing the figures of school incidence; and finally to the other members of the honorary staff of the Royal Alexandra Hospital for Children who agreed to their cases being included in the survey. The clerical staff of the Institute of Child Health, by their cheerful and efficient cooperation, have made possible the publication of the results.

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Reports of Cases.

A CASE OF CHILDHOOD THYROTOXICOSIS.

By D. W. Piper, M.B., B.S.,

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Crile and Crile (1937) stated that thyrotoxicosis in children under five years of age was so rare as to be a medical curiosity. They found four cases in children in this age group among 26,680 cases of thyrotoxicosis in patients admitted to the Cleveland Clinic. Lyons (1949) found only eight cases of thyrotoxicosis in 78,659 admissions to the Children's Hospital, Washington, in thirteen years, and Rankin and Priestley (1932) state that 0·6% of all cases of thyrotoxicosis occur in children before the age of fourteen years. It has, however, been diagnosed in infancy, Klaus (1914) having reported a case in a nine months old baby, and White (1912) an even more unusual instance of hyperthyroidism in a male fœtus. Its incidence increases rapidly at puberty, and the ratio of females to males is seven to one (Kennedy, 1937).

Clinical Record.

S.M., aged five years, had an attack of measles in November, 1950, and after this it was noticed that she became irritable and began to suffer from attacks of vomiting. Next month she developed *otitis media* and this led to an increase in her irritability and vomiting. After three months it was noticed that she had an enlarged thyroid gland and exophthalmos. She did not sleep well and was still irritable and experiencing attacks of vomiting. On June 14, 1951, she was admitted to the Royal Prince Alfred Hospital. She was a slightly irritable child. There was diffuse enlargement of the thyroid gland with a systolic thrill and murmur over it. Her pulse rate was 120 per minute. Her blood pressure was 150 millimetres of mercury, systolic, and 80 millimetres, diastolic. There was no sweating or tremor. Her basal metabolic rate was +23%. After a few days in hospital her emotional state became normal and her pulse rate fell to 90 per minute. As she displayed no signs of thyrotoxicosis she was discharged from hospital to be kept under observation.

After she had been at home for a few days her parents noticed that she was no better. She began to experience attacks of vomiting again, was very irritable and lost weight. Her exophthalmos and thyroid enlargement increased.

She had never lived outside Sydney and investigation of her family history revealed that one aunt had had a simple colloid goitre. As far as could be determined, there had been no emotional conflict at home or at school. Because she was now considered to be in a precritical condition she was readmitted to hospital on August 8, 1951. On examination she was found to be extremely irritable and vomited frequently. There was exophthalmos and diffuse thyroid enlargement. Her blood pressure was 150 millimetres of mercury, systolic, and 70 millimetres, diastolic; her pulse rate was 130 per minute. There was no tremor and no other abnormal endocrine signs were observed. Her weight and height were normal for a child of her age, but her parents noticed that she had rapidly increased in height over the last nine months. Owing to her emotional state, investigations were impossible. She was given 50 milligrammes of methyl thiouracil daily and phenobarbitone, one grain twice daily. At the end of ten days there was great improvement, but her blood pressure had risen to 190 millimetres of mercury, systolic, and 110 millimetres, diastolic, and her pulse rate was still elevated. The thiouracil was increased to 100 milligrammes daily. X-ray examination of her chest and skull and a glucose tolerance test gave normal results. Her bone age was that of a child five years of age.

On September 26, 1951, she was given dried thyroid extract, one-quarter grain daily, but as she again became irritable, with rise in her pulse rate and blood pressure, it was suspended after three weeks. On November 5, 1951, she developed *otitis media*, accompanied by an exacerbation of her symptoms of thyrotoxicosis. She was not gaining weight. The methyl thiouracil was increased to 150 milligrammes daily, and after three weeks of this dosage her skin was dry, she was somewhat lethargic and her basal metabolic rate was −23%. The methyl thiouracil was reduced to 100 milligrammes daily and she is still on this dosage. At discharge from hospital on December 7, 1951, she still had slight exophthalmos, the thyroid gland was much smaller and firm, her pulse rate was 80 per minute, and she was a happy and contented child. Her blood pressure was still 130 millimetres of mercury, systolic, and 85 millimetres, diastolic, and no renal or congenital cause could be found for this slight hypertension. She is now gaining weight. No toxic reactions to methyl thiouracil were encountered.

Figure I.

Showing diffuse thyroid enlargement and exophthalmos present on admission to hospital.

Discussion.

Thyrotoxicosis in childhood is essentially the same as in adults. However, certain features must be stressed as being typical of childhood thyrotoxicosis:

1. The disease is almost invariably primary (Beilby and McClintock, 1937).

2. A predisposing cause, usually an infection, is found more commonly than in adults.

3. The symptoms tend to be more pronounced because of the emotional instability of these young patients.

4. The course of the disease in children is characterized by a greater tendency to remissions and spontaneous cure than in adults.

5. Excessive growth stimulus arising from the pituitary gland or thyroid gland, or from both, causes the onset of symptoms to be often associated with a rapid increase in height (Holmgren)—the bone age often exceeds by several years the chronological age. Tallness and a heavy skeleton may be present in adult life as the sole sequelæ of an oversecretion of the growth factor during thyrotoxicosis in childhood (Reilly, 1940).

6. Elevation of maximum blood pressure and differential pressure is almost constant (Kennedy, 1937).

7. Puberty is often delayed two to four years.

8. Gastro-intestinal symptoms are more common than in adults (Bram, 1944).

The diagnosis in children must be made in most cases on clinical grounds. Basal metabolic rate determinations are unreliable, but protein-bound iodine estimations and the

use of radioactive iodine may help when these are available. Plummer (quoted by Kennedy, 1937) emphasizes the importance of the response to iodine in doubtful cases.

Reilly (1940) stresses the fluctuating nature of the disease in children, in whom the disease occurs in cycles with each cycle less severe and shorter than the previous one, the remissions being not complete until finally spontaneous cure occurs. This benign self-limited type of disease occurred in half of Reilly's cases. However, invalidism and death may result if the disease is not treated.

As regards the differential diagnosis in this age group, exophthalmos may be due to a tumour of the orbit or deformity of the skull such as craniostenosis, and a hypermetabolic state and hypertension may be due to a phæochromocytoma.

The treatment has been revolutionized by the introduction of the thiouracil drugs. For many reasons treatment by drugs, rest and diet is the treatment of choice. Operative treatment carries a considerable mortality, and the results are uniformly poor (Eckel, 1951; Poate, 1951). Post-operative sequelæ, such as hypoparathyroidism and myxœdema, exact a greater penalty in the growing child than in the adult (Topper, 1948). Permanent cardiac damage is rare in children. The thyroid gland is usually not the primary seat of the disease, and post-operative recurrence is common (Topper, 1948). Dosage is regulated according to age and the patient's response as judged by such factors as pulse rate, emotional stability and gain in weight. Surgery is reserved for those rare cases in which the goitre is unusually large, the response to the thio drugs is poor or severe toxic reactions are experienced (Parsons, 1951). Not a single subject of juvenile thyrotoxicosis has been operated on at the New York Hospital since thiouracil has been available (Eckel, 1951). McIntosh (1944) also urges the adequate trial of drug therapy before surgery is advised. Until the question of late cancer following irradiation is settled, it is probably not wise to treat young patients with radioactive iodine, since their life expectancy would include the long latent period necessary for the development of radiation-induced neoplasm (Werner, 1951; Scott, Seaman *et alii*, 1951). McCullough and Richards (1951) have treated a child aged seven years with radioiodine.

The case reported demonstrates certain interesting points relevant to the classical features of childhood thyrotoxicosis. The onset was precipitated by an infection and the disease pursued a course marked by remissions. Rapid increase in height occurred at the onset of the disease. Severe hypertension was a feature of the case and it was the last symptom to disappear. The disease was controlled by methyl thiouracil, and it is hoped that after nine to twelve months' therapy a permanent remission will be obtained. Failure to gain weight may be due to hypothyroidism induced by methyl thiouracil as well as to uncontrolled thyrotoxicosis.

Summary.

1. A case of thyrotoxicosis with the onset of symptoms before the age of five years is described. The patient was treated with methyl thiouracil.

2. The clinical features of childhood thyrotoxicosis are discussed.

Acknowledgements.

I wish to express my thanks to Professor C. G. Lambie for his help in the preparation of this report, and to Mr. Woodward-Smith for the photograph.

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HEPATOSPLENOMEGALY AS A COMPLICATION OF MATERNAL RUBELLA: A REPORT OF TWO CASES.

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Ten years have elapsed since the association between congenital defects and maternal rubella was postulated by Gregg (1941) and confirmed by Swan and a team of South Australian workers (1943, 1944). The main abnormalities reported have been in the heart, the lens, or the cochlea; less common complications reported are mental retardation, mongolism, microcephaly, dental defects, hydrocephalus, cleft palate, hypospadias, congenital obliteration of the bile ducts and diaphragmatic hernia (Dods, 1951).

So far as can be ascertained from the literature, the complication of hepatosplenomegaly with portal hypertension has not been described previously.

Case I.

A female patient, aged eight years, presented at the Brisbane Children's Hospital on October 5, 1949, with a history of abdominal swelling, not increasing in size, of three weeks' duration. Her mother had contracted rubella in the third or fourth month of pregnancy. When the child was three years old the parents were told that she had a congenital heart lesion, but she had never been cyanosed or dyspnœic nor had œdema. When examined she was pale, and two toes of the left foot were fused. The pulse was regular and of good volume, and the apex beat was in the fifth left intercostal space four inches from the mid-line. There was a loud systolic bruit at all cardiac areas with a diastolic bruit to the left of the sternum, and a machinery murmur was heard best in the third left intercostal space. The liver was enlarged to midway between the umbilicus and the rib margin, and the spleen extended to the level of the anterior superior iliac spine. Pathological investigations, including liver function tests, hæmatological investigations and a Wassermann test, gave negative results, apart from microcytic anæmia and persistently low platelet counts (40,000 to 50,000 per cubic millimetre). A diagnosis of patent *ductus arteriosus* and congestive splenomegaly was made, and splenectomy was performed. The findings

were a very large firm spleen and a large liver with very irregular surface, the macroscopic appearance being typical of multilobular cirrhosis. The patient was discharged from hospital, well, five weeks after operation.

Six months later she was readmitted to hospital with ascites and ankle œdema, and a history of dyspnœa of some weeks' duration. She developed a swinging temperature with neutrophile leucocytosis, and *Bacterium coli* was grown on culture from the blood. Death took place five weeks later after a terminal hæmatemesis.

At post-mortem examination the veins at the lower end of the œsophagus were dilated and abnormally prominent; there was a pin-point area of erosion in the mucosa overlying one of them, which appeared to be the likely site of hæmorrhage. The stomach was filled with blood clot, and the small bowel contained blood. The pericardial cavity was distended with yellow-green fluid. The pulmonary trunk was much dilated; there was a short, broad patent *ductus arteriosus* joined to the left pulmonary artery immediately distal to its origin. On the interior surface of the pulmonary trunk there were several pedunculated vegetations firmly adherent to the wall and about four millimetres in length. About the margin of the opening of the ductus into the pulmonary artery there was a further cluster of similar vegetations. The aortic wall was not affected. The heart was enlarged and weighed ten ounces, right-sided dilatation predominating; hypertrophy of both right and left ventricular musculature was present. The *foramen ovale* was closed, and no septal defects were present. The valves were normal. Both lungs contained areas of recent infarcts, as did the left kidney also. The capsule of the liver was in parts thickened, white and opaque. The liver was very nodular, with variety in size and shape of the nodules. It was red-brown in colour, with yellow flecks most pronounced in the nodules, which were present in the greatest number on its anterior and superior surfaces.

Histological examination showed that the fibrous tissue of the portal tracts was increased, with occasional isolation of irregularly sized lobules by dense collagenous connective tissue, few inflammatory cells and little proliferation of bile ducts being evident. There was considerable congestion of the liver sinusoids, with no evidence of fatty change or recent necrosis of the remaining hepatic cells.

Case II.

A male patient, aged nine years, was first examined at the age of three years and reported to have an enlarged liver and spleen and bilateral cataracts. He was then lost sight of till the age of six years, when he was found to have congenital heart disease, gross finger and toe clubbing, poor nutrition with cyanosis, and deafness. When the child was next examined on January 9, 1951, at Princess Margaret Hospital for Children, Perth, at the age of nine years, his mother gave a story of rubella when six weeks pregnant. Two siblings were both well. There had been no history of hæmatemesis or melæna. Examination revealed the patient to be an underdeveloped boy weighing 46 pounds with scaphocephaly and cyanosis of lips and extremities. The heart was not enlarged. A grade II-III systolic murmur was present, most pronounced over the third left intercostal space. Both the spleen and the liver were enlarged; the spleen was palpable a hand's breath below the left costal margin, the liver two fingers' breadth below the right costal margin. Blood examination gave normal results and the Wassermann test produced a negative result. Examination with a barium bolus failed to demonstrate the presence of œsophageal varices. Whilst in hospital he developed infective hepatitis and was jaundiced for about two months. During this illness the serum bilirubin content was 14·8 milligrammes per 100 millilitres, the thymol turbidity was 15 units, and the serum alkaline phosphatase content was 59 King-Armstrong units. On his discharge from hospital four months after admission, the liver was still palpable two fingers' breadth below the right costal margin, but the spleen was smaller on abdominal palpation. His activity had not declined and he was gaining weight, but the prognosis is thought to be poor.

Discussion.

Hepatosplenomegaly is a rare finding apart from well defined causes. Congenital enlargement of the liver and spleen is a rarity. It seems likely that hepatosplenomegaly, with congenital heart disease in both cases, and congenital cataract in the second case, is in the absence of any other cause due to changes taking place *in utero*. In both cases an alteration in early embryonic cell division due to maternal rubella is postulated. In the first case portal hypertension was predominant; this is also likely in the second case, in which a high level of serum bilirubin in the presence of further liver disease would appear to indicate a grave degree of hepatic insufficiency.

Summary.

Two examples of hepatic and splenic enlargement with other abnormalities known to be associated with maternal rubella are described. A search of the literature fails to find a record of this as a complication of maternal rubella.

Acknowledgements.

My thanks are due to the medical superintendent of the Brisbane Children's Hospital and the medical superintendent of the Princess Margaret Hospital for Children, Perth, for permission to report these cases, to Dr. J. J. Sullivan for the histological report in the first case, and to Dr. Felix Arden for his advice.

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Reviews.

A SYLLABUS OF LABORATORY EXAMINATIONS.

"A SYLLABUS OF LABORATORY EXAMINATIONS IN CLINICAL DIAGNOSIS" has been compiled and edited by Thomas Hale Ham, Assistant Professor of Medicine at Harvard Medical School, and Associate Director of the Thorndyke Memorial Laboratory.[1] In his preface, the editor states that the volume was developed over a period of four years, as a part of the second-year course in laboratory diagnosis. The syllabus and a companion volume, "A Color Atlas of Morphologic Hæmatology", are intended "to serve as teaching aids in the diagnosis and treatment of patients, to form a link between preclinical and clinical medicine, and thus to be of assistance to medical students, technicians and physicians". It is dedicated to "the medical students whose enthusiasm and inquiry stimulated its production", and its general arrangement suggests a collection of students' notes, as also do the paper cover and the method of reproduction, namely, offset lithography. "With a low price", writes the editor in his preface, "the syllabus may have a broader usefulness and can be discarded when obsolete." This idea is commendable, but the carrying out of it has its drawbacks. The book reminds one of a telephone book: the cheap paper is bulky and the type is uncomfortable, if not actually difficult to read. This is a pity, for the matter is excellent and written with meticulous care. The syllabus is divided into twenty-seven units, the first three of which deal with tables of normal values, units of measure and the current cost of

[1] "A Syllabus of Laboratory Examinations in Clinical Diagnosis: Critical Evaluation of Laboratory Procedures in the Study of the Patient", edited by Thomas Hale Ham, B.S., M.D.; 1950. Cambridge, Massachusetts: Harvard University Press. 11" x 8½", pp. 508, with three plates and some text figures. Price: 47s. 3d.

laboratory examinations and of apparatus. Units 4 to 16 deal with examinations of blood; units 17 and 18 with examinations related to the urinary system; units 19 to 22 with tests concerned with the gastro-intestinal tract; units 23 to 29 with special tests related to infectious diseases, diseases of metabolism and the examination of extravascular fluids. Lists of references are appended to each unit, and there is a good index. In his preface the editor emphasizes the importance of interpretation and critical evaluation of the limits of accuracy of laboratory tests, wisely pointing out that in the last resort these are the responsibility of the physician.

ANGIOCARDIOGRAPHY.

AN elaborate work entitled "Angiocardiography", being Volume XX of the *Annals of Roentgenology*, has been received from the publishers. It is edited by Charles T. Dotter and Israel Steinberg, and contains all the latest information on the use of X rays in the investigation of the circulatory system. The book is intended for that small number of specialists who deal with cardio-vascular conditions and who have the specialized laboratory necessary for these investigations.

The technique of the examination is dealt with exhaustively in the earlier chapters, but the main value of the work is found in the excellent skiagrams with explanatory line drawings. A 75% solution of either "Diodrast" or "Pyelosil" is used now for angiocardiopathy, it having been found that sodium iodide solutions were too irritating. Even so the method is accompanied by a definite death rate, and thrombosis at the site of injection is quite usual. The method is not regarded as of great use in rheumatic heart conditions. The authors do not consider that the method should be used to the exclusion of the stethoscope. Mediastinal and pulmonary conditions can also be studied by this method.

The work reflects great credit on the authors, but, as stated before, it is essentially a work for specialists within a speciality.

SURGICAL CARE.

"SURGICAL CARE", by Robert Elman, is well described by its subtitle "a practical physiologic guide".[2] It will be useful to any surgeon who wishes to revise and bring up to date his knowledge of the physiology of patients who have undergone a surgical operation or suffered an accidental injury. The book is written by a surgeon whose mind obviously ranges far beyond the carpentry of his art and takes into account not only the physiology but also the mental reactions of the patient. There is much, however, which is tiresome from the point of view of the surgeon, because it describes simple procedures as though giving an account of hospital work to a lay reader.

The author's particular interest is nutrition and homœostasis in all its aspects, and the best parts of the book, including the chapter on burns, deal with this. In assessing the need for protein, or for blood, he stresses the fact that a good nutritional history is a more important guide than laboratory tests. He also stresses the importance of knowledge and judgement in avoiding under-treatment and over-treatment in shock, a point which may well be noted by the house surgeons and even inexperienced anæsthetists who consider this their own province, in which they need not consult the surgeon, even when the latter is readily available. The enthusiasm of the author for nutritional factors sometimes carries him farther than is necessary. For example, even if a well-nourished patient is on a suboptimal diet for two or three days, and therefore likely to lose two or three pounds, the author would feed him intravenously to prevent weight loss. He even finds that salt lack led to the exodus from Egypt and the "conquest of the Pacific" [*sic*]. The book sometimes offends against English grammar and literary elegance; for example, "penicillin has now become inexpensive so that its use is no longer deterred by excessive cost".

[1] "Angiocardiography", by Charles T. Dotter, M.D., and Israel Steinberg, M.D.; 1951. New York: Paul B. Hoeber, Incorporated. 10½" × 8½", pp. 324, with 635 illustrations. Price: $16.00.

[2] "Surgical Care: A Practical Physiologic Guide", by Robert Elman, M.D., F.A.C.S.; 1951. New York: Appleton-Century-Crofts, Incorporated. 10" × 7", pp. 604, with about 60 illustrations and text figures.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"The Medical Clinics of North America"; 1951. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. Philadelphia Number. Three-Year Cumulative Index (1949, 1950 and 1951). 9" × 6", pp. 340, with 27 illustrations and text figures. Price: £7 5s. per clinic year with cloth binding and £6 per clinic year with paper binding.

Contains a symposium on diagnosis in general medicine with 18 articles by 34 authors.

"Physical Medicine and Rehabilitation for the Clinician", edited by Frank H. Krusen, M.D.; 1951. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 10" × 7", pp. 386, with 96 illustrations. Price: £3 1s. 9d.

A text-book for "the average clinician" developed from a series of lectures prepared for the American College of Physicians.

"Clinical and Roentgenologic Evaluation of the Pelvis in Obstetrics", by Howard C. Moloy, M.D., M.Sc.; 1951. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 8½" × 6", pp. 130, with 68 illustrations. Price: £1 3s. 9d.

A monograph based on recent work.

"Principles and Practice of Obstetrics", originally by Joseph B. Delee, M.D., by J. P. Greenhill, M.D.; Tenth Edition; 1951. Philadelphia and London: W. B. Saunders Company. Melbourne: W. W. Ramsay (Surgical) Proprietary, Limited. 10" × 7½", pp. 1030, with 1140 illustrations, 194 in colour. Price: £5 18s. 9d.

The entire book has been practically rewritten.

"Clinical Pediatric Urology", by Meredith Campbell, M.S., M.D., F.A.C.S., with a section on nephritis and allied diseases in infancy and childhood by Elvira Goettsch, A.B., M.D., and John D. Lyttle, A.B., M.D.; 1951. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 10" × 6¾", pp. 1126, with 543 illustrations. Price: £8 11s.

The title explains the contents.

"Clinical Urography: An Atlas and Textbook of Roentgenologic Diagnosis", by William F. Braasch, M.D., and John L. Emmett, M.D.; 1951. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 10" × 7", pp. 742, with 1361 illustrations. Price: £11 17s. 6d.

Written by urologists as a "complete, all-inclusive treatise on urographic diagnosis" for the student or the practitioner.

"Plastic Surgery of the Nose: Including Reconstruction of War Injuries and of Deformities from Neoplastic, Traumatic, Radiation, Congenital, and Other Causes", by James Barrett Brown, M.D., and Frank McDowell, M.D.; 1951. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 10" × 7", pp. 428, with 379 illustrations, 48 in colour. Price: £7 17s. 6d.

A "practical clinical book" based on personal experience.

"Patterns of Sexual Behavior", by Clellan S. Ford, Ph.D., and Frank A. Beach, Ph.D., with an introduction by F. A. E. Crew, M.D., D.Sc., Ph.D., F.R.S.; 1952. London: Eyre and Spottiswoode. 9" × 6", pp. 314, with 16 text figures. Price: 22s. 6d.

A comparative study of sexual behaviour patterns as found in 109 contemporary human societies.

"Metabolic Interrelations: Transactions of the Third Conference, New York, January 8-9, 1951", edited by Edward C. Reifenstein, Junior, M.D.; 1951. New York: Josiah Macy Junior Foundation. 9¼" × 6¼", pp. 294, with 85 illustrations. Price: $4.00.

Contains 15 papers with accompanying discussion. All relate to bone or cartilage.

The Medical Journal of Australia

SATURDAY, APRIL 12, 1952.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

LEONARDO DA VINCI.

In the present year, 1952, the fifth centenary of the birth of Leonardo da Vinci will be celebrated. Leonardo was the son of Ser Piero, a notary; his mother was a peasant named Caterina. The exact date of his birth is not known, but official celebrations will take place in Italy beginning on April 15, 1952, and extending until the end of the year.[1] On April 15 an exhibition of drawings, autographs and documents concerning Leonardo da Vinci will be opened at Florence in the library "Mediceo-Laurenziana"; the exhibition will be open until October 30. The work of restoration of the house in which Leonardo was born in 1452 at Anchiano, a village near the little town of Vinci, has been undertaken. The celebrations are in the hands of a national committee presided over by Signor Marazza, a member of the Italian Parliament; they will commence at Vinci on April 15 and continue during the year at Rome, Venice, Bologna, Genoa, Florence, Parvia and Milan. At Milan in the old cloister of San Vittore an exhibition will be held. Commemorations of Leonardo da Vinci are also being organized in France, England, Germany, the United States of America, Argentina, Mexico, Ecuador and Chile. Leonardo was unique and preeminent in thought, word and work; he accomplished so much in every sphere of life that he touched, that he has been described as an exemplar of *"l'uomo universale"*. There has been no one like him, and the more we read about him, the more amazing he becomes. The range of his interest covered art and science and philosophy. In art he was painter, sculptor, architect and musician; in science he was an anatomist marking a new epoch, and an engineer, civil and military, showing things that would come after him, including aviation; his famous "notebooks" reveal him as a philosopher of rare understanding. In his own time he was as a bright light shining in the darkness; many tried to imitate him, and authors through the ages have sought to fathom the depth of his wisdom and discover the many facets to his character. It is fitting that the civilized world should pause during the present year to contemplate this peerless man and to honour his memory. Medicine is both an art and a science; those who follow medicine as a calling have therefore a twofold reason for celebrating the fifth centenary of Leonardo da Vinci's birth.

Leonardo's birth year is known to be 1452 from a taxation return made in 1457 by his grandfather, Ser Antonio, in which he numbers those residing in his *casa* at Vinci. The residents included Ser Piero, thirty years of age, and Piero's young wife Albiera. There was also Leonardo, aged five, the illegitimate son of Ser Piero; Leonardo's mother, Caterina, had married Chartabrida di Piero del Vaccha da Vinci. In 1469 the family moved to Florence. Ser Piero, the notary, was successful in his practice, and we are told that he probably used his professional influence on behalf of his brilliant son, and that this may explain to some degree why Leonardo was so perversely cavalier towards his early Florentine commissions. Ser Piero had been intelligent enough to give his son a magnificent name, and to take his early drawings to his friend the painter Verrocchio. The latter was astonished by the quality of Leonardo's work, and received the boy as a pupil when he was fourteen years of age. At the age of seventeen Leonardo was living independently among various companions, and earning a great reputation for versatility, grace and power. In all accounts of Leonardo we read of his personal beauty. Kenneth Clark, in his Ryerson Lectures of 1936, states that Leonardo was beautiful, strong, graceful in all his actions, and so charming in conversation that he drew all men's spirits to him. Vasari describes his love for and mastery of horses, and tells how he would buy birds in the market place, take them in his hand and let them go to give them their lost liberty. The almost magical powers with which he was credited in old age were interpreted as part of his physical perfection. Kenneth Clark regards this interpertation as naïve and incomplete, but thinks that it contains one small part of truth. Another fragment, which Clark describes as of an almost contrary kind, will be of interest to medical folk. It concerns a symbolic dream described by Leonardo in one of his "notebooks". He wrote: "In the earliest memory of my childhood it seemed to me that as I lay in my cradle a kite came down to me and opened my mouth with its tail, and struck me many times with its tail between my lips. This seems to be my fate." Clark rightly remarks that we are still too ignorant of psychology to interpret such a memory with any finality, but adds that it is not surprising that Freud took this passage as a starting-point for a psychological study of Leonardo. It is not necessary to describe Freud's study in any detail, but it will suffice to record Clark's statement that Freud's conclusions have been rejected with horror by the majority of Leonardo scholars—"the workings of a powerful and complex mind cannot be deduced from a single sentence or explained by a rather one-sided system of psychology". Most of us would agree with Clark that Freud's study is possibly an over-simplification, but that it helps our conception of Leonardo's character by insisting that he was abnormal.

It is unnecessary in this place to attempt any full account of the life of Leonardo da Vinci; every modern

[1] Information about the celebrations has been kindly supplied by the Italian Legation, Sydney.

library is full of books dealing with his life and the many aspects of his work. As medical men and women, readers of this journal will be particularly interested in Leonardo as an anatomist. Professor J. P. McMurrich, himself an anatomist, concludes that Leonardo initiated a new movement in anatomy, and one destined in time to replace piece by piece the old foundations by more substantial ones. The inauguration of a revolution in descriptive anatomy ranks him as a great anatomist, and his right to that title is confirmed by the many important discoveries he made in following out his methods. McMurrich points out that he is guilty of many errors of omission and commission, but that these may be ascribed in part to his preoccupation with many other interests and in part to the influence of his Arabistic foundations. He declares that on the opposite page, however, are to be placed to his credit important discoveries, the harvest of his reliance on observation. It is important to remember that Leonardo carried out dissections on animals and on man. Pictures of his dissections are reproduced in many books about him. McMurrich has chapters on Leonardo's work on the skeleton, the muscles, the heart, the blood vessels, the organs of digestion, the organs of respiration, the excretory and reproductive organs, the nervous system, the sex organs, embryology and comparative anatomy as well as botany. He mentions particularly Leonardo's observation of the correct inclination of the pelvis, his discovery of the frontal and maxillary sinuses, his discovery of the moderator band of the heart, of the bronchial arteries and of arterial sclerosis, and his rediscovery of the thyroid gland and of the unilocular structure of the uterus. More striking than these, McMurrich thinks, is Leonardo's emancipation from belief in the theory of innate heat; it was striking because it was the denial of one of the fundamental tenets of antiquity, and because it illustrated a characteristic striving to explain phenomena on the basis of a natural rather than a supernatural causation. Leonardo was distinguished from his mediæval predecessors and from his contemporaries in anatomy by his greater desire for thoroughness. When he wanted to keep a record of a dissection, he was not content with one drawing, but made several of the same part; these may be seen in many of the reproductions of his work. Having assigned to Leonardo high rank as a scientist and an anatomist, McMurrich asks what is his status in the history of anatomy. He thinks that the fact that his discoveries were not published and so given to the world at large undoubtedly lessened his influence on the progress of anatomical knowledge, but he adds that this influence cannot have been entirely lacking. His fellow artists must have known of them, and so too his fellow members in the Florentine Guild of Physicians and Apothecaries, and there are reasons for a belief that his anatomical drawings were known far beyond the confines of Italy. It is pointed out that certain drawings in Albrecht Dürer's sketch books were undoubtedly copies of drawings by Leonardo. McMurrich thinks that it is worthy of note that the foundations for modern descriptive anatomy were laid in northern Italy, where Leonardo's influence would be most readily felt. In this regard it is interesting that in a chapter on Leonardo as anatomist, E. Hopstock, writing in "Studies in the History of Method of Science", describes Leonardo as "the first to have illustrated anatomy by drawing from the object, the first of the moderns to have treated anatomy in a methodical and scientific way by means of independent research and post-mortem dissection". Hopstock describes Leonardo as "a modern biologist in the disguise of a mediæval artist". He discusses *inter alia* Leonardo's investigations of the heart and blood vessels. He thinks that in spite of omissions and errors, Leonardo had a fairly correct conception of the circulation. Two quotations from Leonardo's "*Fogli*" support this statement:

> By the ramification of the veins in the mesentery, the food is drawn from the corruption of the aliments in the intestines, and eventually is returned by the ultimate ramification of the arteries to these intestines. . . .
>
> The origin of the sea is the contrary of that of the blood, for the sea receives in its bosom all the rivers, which are produced only by the vapours of water, risen into the air: the sea of the blood is the cause of all the veins. The aorta is only one which subdivides into as many principal branches as there are principal parts to be nourished, branches which continue to ramify *ad infinitum*.

A great deal might be written about Leonardo's activities in the field of engineering. His extraordinary mind covered a wide range, and included military and civil requirements. The kind of thing with which he concerned himself is shown in a letter written by him to Lodovico Sforza, who afterwards became Duke of Milan. Leonardo applied to Lodovico for a position as a military engineer. His letter is reproduced in full by W. R. Parsons. In this letter Leonardo recommends himself in three capacities. First, he sets out in detail what he is prepared to do as a military engineer. He can construct bridges which are light and strong and capable of easy transportation; he can make others which are safe and capable of resisting attack and fire, and which are easy and convenient to place and remove. He knows how in a place under siege to remove the water from moats and make infinite bridges, trellis work, ladders and other instruments suitable for the purpose. Also he has means of destroying fortresses or fortifications not built of stone. He has a means of making cannon easy and convenient to carry, and with them to throw out stones similar to a tempest, and with the smoke from them to cause great fear to the enemy, to his grave damage and confusion. He describes many other types of military equipment, such as wagons, dart throwers and fire-throwing machines and methods of tunnelling and creating secret passages. As a civil engineer he states that he can give satisfaction in architecture and in the designing of public and private edifices, and in conducting water from one place to another. In addition he offers to undertake sculpture, and suggests that he shall start work on a bronze horse to the memory of the illustrious House of Sforza. Lodovico invited Leonardo to enter his service. Leonardo studied the flight of birds, and from these he deduced some of the principles whose modern application has made aviation possible. Parsons reproduces the following five:

1. Flying is due to air resistance, and the air exercises as much force on an object as an object does on the air.
2. There are two centres, that of gravity and that of pressure, and their relative position to each other must be adjusted to secure equilibrium.
3. There are air currents too fine for human detection, whose existence and movement birds are able to observe and utilize by soaring and drifting with wings outstretched and motionless.
4. Birds' wings have been made by Nature convex above and concave below so as to facilitate upward flight.

5. Hills and other surface variations produce "air eddies and whirlwinds", or what aviators now call "pockets".

What Leonardo lacked was a motor by which he could drive himself with stationary wings, and so make use of the first of his conclusions. The world waited more than four hundred years for the motive force which Leonardo lacked.

Only brief reference need be made to Leonardo's painting, for it is as a painter that he is best known. To extol his work is unnecessary, and indeed would be almost an impertinence. Most people have seen reproductions of his wall painting "The Last Supper", and also of his "Mona Lisa". These are probably the two best known of all his works. "The Last Supper" was painted on the wall of the refectory of the Convent Church of Santa Maria della Grazie at Milan. In spite of the fact that it has had to be restored more than once, it still attracts hundreds of what may be described as pilgrims who visit Milan specially to see it. Of the "Mona Lisa" a great deal has been written, some of it sense and some of it nonsense. It is a picture round which speculation may have an infinite variety; much argument can be worked up about it, and, as in so many other things, the argument will probably reveal more about those who take part in it than about the picture itself. It is probably the most widely discussed picture in Europe, and that is all that need be said about it at present.

We have glanced at Leonardo da Vinci's superb and many-sided achievements. What of the man himself? One author has described him as a standing refutation of the belief that all great men are simple, because in actual fact no more complex and mysterious man has ever existed. In our study of him it is always necessary to be on guard that imagination does not take charge and lead to unwarranted fantastic conclusions. This appears to have been done by some authors who have written about him. He lived in a society which may be described as extravagant and licentious, but while he was in it he appears not to have been of it. Probably his creative genius and his power of interpretation crowded other things out of his life. Women to him were creatures to be painted and not to be loved. He had an artist's insight, but it is said that he gave to some of his subjects qualities which were not really there, but which he chose for them. From his "Notebooks" some passages may be quoted:

Experience is not at fault; it is only our judgement that is in error in promising itself from experience things which are not within her power.

Again:

As a well spent day brings happy sleep, so life well used brings happy death. While I thought I was learning how to live, I have been learning how to die.

We may conclude with the following:

Great love is born of great knowledge of the objects one loves. If you do not understand them, you can only admire them lamely or not at all—and if you only love them on account of the good you expect from them, and not because of the sum of their qualities, then you are as the dog that wags his tail to the person who gives him a bone. Love is the daughter of knowledge, and love is deep in the same degree as the knowledge is sure—Love conquers all things.[1]

[1] In the compilation of this article the following works have been consulted: "Leonardo da Vinci", by Kenneth Clark; "Leonardo da Vinci's Notebooks", by Edward McMurdy; "Art and Scientific Thought", by Martin Johnson; "Leonardo the Florentine", by R. A. Taylor; "Studies in the History and Method of Science", edited by C. Singer; "Engineers and Engineering in the Renaissance", by W. R. Parsons; "Leonardo da Vinci the Anatomist", by J. B. McMurrich; "The Mechanical Investigations of Leonardo da Vinci", by I. B. Hart; "The Renaissance", by Walter Pater; "Leonardo da Vinci", by Georg Gronau; "The Encyclopædia Britannica", Fourteenth Edition.

Current Comment.

THE INTRAVENOUS ADMINISTRATION OF PROCAINE FOR RELIEF OF PAIN.

In a preliminary report published in 1947, D. J. Graubard and H. H. Ritter[1] described the results of the intravenous administration of procaine in the treatment of patients with various traumatic conditions. They stated that it had been proved that procaine given intravenously would be concentrated seven to eight times more in traumatized tissue than in normal tissue, and they presented evidence to suggest that interference with the reflex arc established after trauma would hasten the recovery and rehabilitation of the injured person. Their view is that the response of the tissues which follows trauma is a defence mechanism. The vasospasm and the exudate which are found at the site of trauma subside in the majority of instances at the conclusion of the healing process. If, however, the vasospasm and the œdema persist, an irritative focus is said to exist. In most of their patients they believed that they were able to alter the reflex arc which produced these manifestations, so that pain, spasm and œdema were reduced. They believed also that the healing process was accelerated. Since 1947, almost fifty publications have appeared, which report that many varieties of pain as well as œdema, muscle spasm, itching, symptoms of asthma and certain eye diseases have been relieved by the intravenous administration of procaine. Most observers have reported that the side actions are minimal and of little consequence. In referring to this, A. S. Keats, G. L. D'Alessandro and H. K. Beecher point out that, despite the necessity of controls in investigations of this type, no observer known to them in studying the beneficial effects of the drug has treated a comparable group either with a placebo or with a standard therapeutic agent.[2] In addition, they state, the known rapid hydrolysis of procaine in the blood-stream and the slight or absent analgesic effects of its breakdown products (para-aminobenzoic acid and diethylamino ethanol) are not in accord with the prolonged pain relief reported. For these reasons they undertook a control study of pain relief by the intravenous administration of procaine, and the Council on Pharmacy and Chemistry of the American Medical Association has authorized publication of their report on the study. Their subjects were 53 patients who had undergone major surgical procedures and who developed constantly present wound pain of moderate or severe degree on the first day after operation. When a suitable degree of pain developed, the patient was given the first drug of a series (saline, procaine, morphine), and the degree of pain relief was evaluated at specific intervals thereafter (usually thirty and sixty minutes). If little or insufficient relief was obtained, the second drug was given and its effect again evaluated at specific intervals. The third drug was given and evaluated similarly. If pain relief was obtained after any dose, the subject was observed at intervals until his pain returned to approximately the original level, and then the series of drug administrations was continued as described. Procaine was given in a strength of 0·1% in a 5% solution of dextrose in water through an intravenous infusion set. Saline was given in a similar manner at a rate of approximately 200 millilitres per hour. Morphine was injected slowly by the intravenous route over the course of one minute; the dosage was always eight milligrammes per 70 kilograms of body weight. A medical observer recorded side actions, and care was taken to maintain a standard technique. The effects of drugs were judged by their ability to produce both pain relief and comfort, the efficacy of any single dose of a drug being evaluated in terms of four possible categories: (*a*) no comfort, no pain relief; (*b*) no comfort, pain relief; (*c*) comfort, no pain relief; (*d*) comfort, pain relief. The results are set out in detail and analysed in the report. In summary, it was found that the intravenous

[1] *The American Journal of Surgery*, November, 1947.

[2] *The Journal of the American Medical Association*, December 29, 1951.

administration of procaine relieved 40% of patients, in contrast to 20% with saline and 70% with morphine. These differences are stated to be statistically significant, despite the relatively small number of patients. Further, the percentage of patients relieved by morphine is probably a low estimate, since morphine was given primarily to patients not relieved by saline or procaine. The degree of relief produced by procaine is stated by Keats and his colleagues to approximate that produced by the administration of 90 milligrammes of pentobarbital sodium. However, such analgesia as procaine did produce was achieved at the cost of tremendous side action, mainly unpleasant. Keats *et alii* regard as alarming the effects experienced by some patients—extreme anxiety and apprehension, dyspnœa, tachycardia (to 150 per minute), disorientation and violent vomiting. They state that in six cases the administration of procaine had to be stopped because of the magnitude of the side actions. Patients begged to have the infusion stopped because of the unpleasantness, and some wept when anticipating a repetition; but an equal number enjoyed its effects. It is conceded that the doses used may have been excessive, and therefore the side actions excessively frequent and severe. However, as is pointed out, the low degree of analgesia attained even with these doses, and the possibility of such side actions with small excesses in dose do not enhance the usefulness of the drug. Obviously it is not a substitute for morphine. A further disadvantage is that the rapid administration of the large volumes of fluid necessary for this therapy complicates post-operative fluid balance, especially in patients who have undergone abdominal surgery and in those with heart disease. The use of more concentrated solutions decreases the safety and controllability of the procedure. In general, the advantages of the intravenous administration of procaine appear to be greatly outweighed by the disadvantages. The study itself provides good evidence of the need for controls in investigations of this type.

INDUSTRIAL MEDICINE ON THE PLUTONIUM PROJECT.

WHEN early in 1942 it was apparent that a nuclear chain-reacting pile could be built, the enormity of the health hazards which such a unit would create was realized. The exact nature of the hazards to be encountered was not known. In general it was realized that the pile in which the chain reaction would take place would be a far greater source of fast and slow neutrons and γ rays than could have been imagined in earlier periods. It was estimated that the pieces of uranium which would have to be removed from the pile after fission had occurred would contain materials far more radioactive than any that had been encountered in the radium industry. It appeared certain that not only the uranium, but also other material that would be removed from such a pile would be extremely active in producing α, β or γ rays. The chemical processes of separating the plutonium from the other extremely radioactive substances was recognized as an extremely hazardous procedure. The effect that plutonium itself might have on the workers was unknown.

Since the magnitude of the hazards involved in the physical and chemical procedures was unknown it was recognized that the planning committee would have to include a wide range of scientists. Such a committee was set up, and it gradually evolved into an organized health division. Its members had to work out methods for the protection of the health of the workers on the project and for the protection of the public, and to study the peculiar hazards in order better to establish tolerance doses, to predict more accurately what might happen in the future, to devise methods for detecting ill effects to personnel and to discover methods for treating any person who might be injured. The results of their activities, in so far as they are concerned with the medical aspects of the question, are set out in detail in "Industrial Medicine on the Plutonium Project", edited by Robert S. Stone.[1] This book consists of an introduction, ten surveys on different aspects of the problem and ten papers on special researches. Much of the matter is very technical, but much of it is of general medical interest. We are told that every person on the project was given an extremely thorough medical examination before employment. If there were no medical defects the prospective employee was cleared for all areas. If there were physical handicaps an attempt was made to place the person concerned where he would be most useful, and definite restrictions were imposed on the type of work he was permitted to do. Before transfers took place from one plant to another or to another part of a plant, another thorough examination was made. So far as possible periodical examinations were made of all employees. Even visitors to the most important plants had to produce satisfactory evidence of good health. Every possible precaution was taken to prevent over-exposure to radiation. This involved not only the physical protections in the plant, but also the training of employees in proper techniques for handling active substances.

Disposal of unwanted radioactive substances has been, and continues to be, a major problem. The precautions used are set out in detail in this book. All employees carried special badges with film in them which would detect the quantities of radiation to which they might be exposed. So good were the precautions that no employee working at the largest unit of the project—the Hanford Engineer Works—received an amount of radiation exposure which would be injurious. When work on nuclear fission commences on a large scale in Australia, the information contained in this book and the companion volumes will be of great value.

THORACO-LUMBAR SPLANCHNICECTOMY AND HYPERTENSION.

R. H. SMITHWICK has been interested in the problem of the surgical treatment of hypertensive cardio-vascular disease for over seventeen years, and since 1938 has been employing a standardized surgical procedure, thoraco-lumbar splanchnicectomy. Some 3000 patients have been referred to him for consideration of surgical treatment. Of these, approximately two-thirds have been operated on, and one-third have been treated medically, and he has now published a paper in which he discusses the effect of thoraco-lumbar splanchnicectomy on the mortality rates and survival rates of those patients who have been followed sufficiently long for the results to be of value.[2] He considers that the majority of his patients have not been followed long enough to be included in the discussion at present; but he is able to write of 892 patients who were treated during the years 1938 to 1946 inclusive, and who have been followed for at least four and at most twelve years. The basis of his paper is a comparison of the results of surgical and non-surgical treatment. Comparison studies based on large unselected groups of patients with hypertension are unsatisfactory, as the prognosis varies tremendously in accordance with the patient's initial condition. For this reason Smithwick has found it necessary to group his patients, and has used the systems of classification used by two other groups of authors as well as his own. It appears that if patients are classified into four groups according to the criteria of Keith, Wagener and Barker—criteria based essentially on examination of the ocular fundi—the findings indicate that the mortality rates have been significantly lowered in all groups as a result of thoraco-lumbar splanchnicectomy. Again, if patients are arranged in a different fashion into various groups according to the amount of cardio-vascular damage in the cerebral, retinal, cardiac and renal arteries, it

[1] "Industrial Medicine on the Plutonium Project: Survey and Collected Papers", edited by Robert S. Stone, M.D.; First Edition; 1951. New York: McGraw-Hill Book Company, Incorporated. 9" × 6½", pp. 536, with 32 illustrations and many text figures.

[2] *The Journal of the American Medical Association*, December 22, 1951.

appears from the findings of Hammarström and Bechgaard that life expectancy has been improved by surgical treatment. For his own 892 patients, Smithwick has adopted an original system. He explains that operation was suggested to the patients as offering a reasonable or a slight chance of worthwhile result according to the states of their cardio-vascular systems when first studied. The majority of the patients elected to be operated on. Those who decided to follow a medical régime make up the control series. The patients were divided into four groups on a plan designed to control as many of the variable factors as possible. After a careful study of the cardio-vascular system as a whole, a numerical value is assigned to various factors which have a bearing on prognosis. The numerical values for each factor present are totalled, and this gives the numerical grade for the patient. The numerical grade, together with certain other factors relating to the state of the eyegrounds or to certain other particular features of the cardio-vascular system, determines the group. A comparison of the results according to this system indicates that the prognosis for patients in three of the four groups has been significantly improved by thoraco-lumbar splanchnicectomy. These patients had cardio-vascular changes ranging from slight to severe. While the mortality rate for patients in the other group is lower for those treated surgically than for the control series, the difference has not as yet become statistically significant. Smithwick expects that it will become so with a longer period of observation. He considers that severe kidney damage, as indicated by persistent evidence of nitrogen retention, is the one finding which contraindicates splanchnicectomy in the more advanced stages of cardio-vascular disease. The great majority of the patients treated surgically, as well as the controls, were middle-aged; approximately 90% were under fifty years of age, and 80% were between twenty and forty-nine years of age. Smithwick's classification is somewhat complicated, and some will possibly regard it as clumsy. Nevertheless, it embodies an attempt to bring all the relevant factors into the picture. It appears to have served well in assessing the results of past experience, and from that point to provide a useful basis for the selection of patients for splanchnicectomy.

BERYLLIUM POISONING.

BERYLLIUM POISONING has received a good deal of attention, especially in industrial health circles, during the past five years or so. Although some aspects of the subject remain obscure, valuable progress has been made in the understanding and management of this disease, which is essentially an occupational condition, apart from the occasional case of beryllium granuloma following a cut with glass from a broken fluorescent lamp. According to H. S. Van Ordstrand,[1] beryllium has been called the "glamour child" of metallurgy. A metallic element, recognized more than 150 years ago, it and its salts have found a wide application in industry. Beryllium metal is lighter than aluminium, extremely penetrable to X rays, a remarkable transmitter of sound and an excellent source of neutrons; it is used in the "window" for X-ray tubes and in nuclear physics developments. Beryllium oxide has a melting point of 2570° C., is an excellent insulator at high temperatures, has unusual resistance to thermal shock and has high thermal conductivity; it has been used in the making of high temperature crucibles, in ceramics, in the "phosphor" in neon tubing and in fluorescent lights, though here it is being discarded, and in cathode heating elements in radio tubes. The addition of only a small amount of beryllium to copper produces a particularly useful alloy. Thus it is used widely and many workers come into contact with it in various forms. Ordstrand states that the medical hazard from beryllium has been reported as occurring throughout its use, except in the fields of mining, handling and shipping as related to the ore beryl. Beryllium metal (particularly in its machining) and beryllium compounds have been the cause of the clinical disease. Beryllium poisoning or berylliosis is defined by W. Machle, E. Beyer and F. Gregorius[1] as "a general disease characterized clinically by pulmonary insufficiency and with the major pathological changes in the lung"; it results from inhalation of finely divided beryllium compounds. The other common manifestations occur in the skin, either as contact dermatitis from beryllium salts or as subcutaneous granuloma from introduction of beryllium compounds under the skin. The lung condition is acute or chronic, manifestations of the latter form appearing in some cases as long as ten years after exposure to beryllium. The essential condition appears to be systemic rather than local in the lung. From the diagnostic point of view it is important to note that in 98 cases of pneumonitis (so-called acute cases) observed by Ordstrand and those working with him, the X-ray changes have invariably followed the onset of a relatively non-productive cough and progressive dyspnœa by two or three weeks on the average. On the other hand the X-ray changes in a number of cases of chronic lung involvement have been evident prior to the onset of symptoms (cough, dyspnœa, anorexia, weight loss), or at least prior to the onset of noticeable ill health. Machle and his colleagues list the essentials for the diagnosis of beryllium poisoning as a significant history of exposure, occupational or otherwise, a characteristic clinical pattern with consistent laboratory and X-ray findings, and the finding of beryllium in tissues or urine. The mortality rate associated with the acute form in Ordstrand's experience is 12 deaths in 98 cases; the total duration of illness in non-fatal cases has not exceeded four months. The rate is higher in chronic cases; one-third of the patients have died, and of the remaining two-thirds, one-third have shown progressive deterioration, with the exception of those having ACTH therapy. The pathological feature of the acute disease is essentially intraalveolar œdematous exudate; death results from asphyxia. In the chronic form the lesions are predominantly interstitial, chronic and granulomatous; the myocardium on the right side of the heart is hypertrophied, and death is due to chronic *cor pulmonale*.

Ordstrand quotes the work of G. H. Curtis[2] as a clear demonstration of the fact that the eczematous-contact type of dermatitis in beryllium workers is a hypersensitization phenomenon. Curtis also inclines to the view, as does Ordstrand, that the acute lung condition may be an allergic reaction. Work on the pathogenesis of the chronic form, both in the United States and in Great Britain, suggests that beryllium has an inhibitory effect on the alkaline phosphatase enzymes. The hypothesis has also been put forward that beryllium may compete for magnesium in magnesium-activated enzymes.

Until the introduction of ACTH and cortisone, therapy was unsatisfactory. Oxygen has been of most value, but its effect was apparently symptomatic only. Many instances have now been reported of benefit from ACTH and cortisone medication, though its ultimate value cannot yet be assessed. L. Roche *et alii*[3] had three patients with acute lung involvement in severe degree. One died. The other two were treated with cortisone and responded rapidly; recovery is apparently complete, but they are to continue under observation. E. M. Kline *et alii*[4] reported a favourable response in five subjects of chronic beryllium poisoning treated with ACTH or cortisone. In seven cases of beryllium granulomatosis from various sources quoted in "The 1951 Year Book of Medicine", response to ACTH was satisfactory, but, as in all cases reported, a longer period of observation is necessary. It must be mentioned in conclusion that the incidence of beryllium poisoning is lessening because of control measures in industry; these, in Ordstrand's opinion, are eliminating it as an important medical problem.

[1] *Annals of Internal Medicine*, December, 1951.

[1] *Occupational Medicine*, June, 1948.

[2] *A.M.A. Archives of Dermatology and Syphilology*, October, 1951.

[3] *Archives des maladies professionnelles de médecine du travail et de securité sociale*, Number 6, 1951.

[4] *A.M.A. Archives of Industrial Hygiene*, June, 1951.

XUM

Abstracts from Medical Literature.

DERMATOLOGY.

Interdigital Syphilitic Lesions Simulating Dermatophytosis.

H. T. Dexter (*Archives of Dermatology and Syphilology*, May, 1951) reports a series of ten cases in which the lesions of secondary syphilis resembled dermatophytosis of the feet. In two of these a local Herxheimer reaction occurred after the first therapeutic injection of penicillin. Points of differential diagnosis of syphilitic interdigital lesions and epidermophytosis are given in a table. The author states that the interdigital lesions have in all cases epithelialized and disappeared rapidly after penicillin therapy without any topical medication. In epidermophytosis there has usually been chronic scaling with cracking of the skin on the feet and between the toes preceding the onset of the ulceration. The rare case of epidermophytosis with ulcers as extensive as those found in syphilis is accompanied by more œdema, erythema and induration of the surrounding tissues. Cellulitis and lymphangitis are usually present. The ulcers of epidermophytosis are less sharply demarcated, shallower and more irregular in depth; the appearance is that of spotty superficial erosion. The bases are less red. Evidence of scaling and maceration of adjacent tissue is usually found. Lymphadenopathy, if present, is limited to the inguinal nodes of the involved side, in contrast to the more generalized lymph node enlargement which is usually present with secondary syphilis.

Bacitracin in Dermatology.

E. F. Finnerty (*The New England Journal of Medicine*, July 1, 1951) presents clinical data obtained after bacitracin topical therapy for a large variety of accessible pyodermas. He states that in many cases there had been no response to other therapeutic routines. Response to either an ointment consisting of 500 units of bacitracin per gramme of petrolatum or compresses with an optimal concentration of 500 units per millilitre was rapid and effective and led to no recurrence in an astonishing number of cases. Cures were effected in 61·5% of cases. The wide variety of infections presented by the entire group indicates that the therapeutic value of bacitracin is applicable in topical therapy to all pyogenic skin disorders caused by staphylococci and streptococci. The author found a low incidence of allergy to bacitracin.

Dermatitis with Lipomelanotic Reticular Hyperplasia of Lymph Nodes.

T. C. Laipply and C. J. White (*Archives of Dermatology and Syphilology*, May, 1951) report fifteen cases of dermatitis with lipomelanotic reticular hyperplasia of lymph nodes. They state that the association of a peculiar type of hyperplasia of lymph nodes with chronic dermatitis was first fully discussed in 1937. The dermatitis varied in type and degree, but was usually erythematous, desquamative, of localized distribution and associated with pruritus. The lymph node hyperplasia was characterized by multiplication of reticular cells, the presence of intracellular fat and melanin pigment, and slight infiltration of eosinophile cells. Clinically cases were suspected of being possibly in the lymphoblastoma group, Hodgkin's disease, *mycosis fungoides* or lymphosarcoma. Proper analysis of the histological features of the granulomatous character of the lymph nodes pointed in all cases to a benign reactive process. That a progressive lymph node disease was absent was substantiated by prolonged follow-up observation. Chronic dermatitis, particularly when accompanied by pruritus, may result in a characteristic type of hyperplasia of lymph nodes, which are usually moderately enlarged, discrete, firm and not tender. The microscopic features include slight distortion of the normal architectural pattern, severe hyperplasia of reticular cells, which contain melanin and sudanotropic droplets, and infiltration with eosinophile cells. Because of the presence of the lymphadenopathy an incorrect diagnosis of lymphoblastoma may be made in many instances. Although it may be associated with leuchæmia, Hodgkin's disease or lymphosarcoma, the condition has no direct relationship to them.

Acrodermatitis Pustulosa Perstans.

H. C. Fishman (*Archives of Dermatology and Syphilology*, July, 1951) describes a method of treatment for *acrodermatitis pustulosa perstans*. He states that diversity of opinion as to its ætiology is emphasized by the other synonyms, namely, pustular psoriasis of Barber and pustular bacterids of Andrews. The ætiology is still unknown. The patients treated had lesions with the typical clinical appearance—tiny, deep-seated vesiculopustules studding erythematous, slightly scaly patches in the palms and soles. Biopsies showed the histopathological picture to be that of a large pustule in the prickle-cell layer, filled with polymorphonuclear leucocytes and cellular debris. There was no thinning of the suprapapillary plates and no elongation or clubbing of the rete pegs. Culture and slide examinations failed to reveal fungi. No patient had signs of psoriasis elsewhere. Ten consecutive patients were cleared of *acrodermatitis pustulosa perstans* by the daily administration of 150,000 units of vitamin *A*, the frequent application of 5% coal tar solution in a water-soluble base, and weekly administration of radiation from a cold quartz lamp.

Lichen Simplex Chronicus (Vidal) Treated Successfully with Podophyllin.

J. Garb (*Archives of Dermatology and Syphilology*, June, 1951) reports the result of treatment with podophyllin in seven cases of circumscribed neurodermatitis. The preparations used were a 0·25% to 10% strength ointment and a 0·5% to 2% solution in 70% alcohol. The skin beyond the edges of the lesion was coated with flexible collodion to protect the unaffected area. The ointment was applied at weekly or twice-weekly intervals and the site of application covered with waxpaper and bandaged for twenty-four hours; then a salve was applied containing bismuth subgallate two parts, castor oil four parts and white petrolatum sufficient to make thirty parts. The author lists the following advantages of podophyllin: (i) it reduces lichenification; (ii) itching is quickly relieved; (iii) the benefits are long-lasting; (iv) podophyllin treatment may be repeated without injury to tissue. He states that corneal damage due to accidental contact with podophyllin must be borne in mind. The results of treatment compare favourably with those of X-ray therapy.

Occupational Leucoderma from Rubber Dust and Debris.

S. J. Zaton and A. L. Goldberg (*Archives of Dermatology and Syphilology*, October, 1951) state that cases have been recorded by Spencer of leucoderma due to "Agarite Alba", the trade name of the antioxidant monobenzyl ether of hydroquinone in rubber. Recently the authors have encountered nine cases of leucoderma in white workers who come in contact with dust and debris containing "Agarite Alba". These workers are machine operators who sew thin rubber strips onto asbestos pads. In the course of the operation a heavy alkaline oily dust is created; this settles down upon the face, hands and forearms of the workers, and in some of the workers causes areas of depigmentation. Leucoderma has developed in only nine of 200 workers, all of them white and similarly exposed. Other factors besides mere contact are needed to produce this phenomenon.

Allergy to Pituitary Corticotrophic Hormone.

S. M. Feinberg, A. R. Feinberg and E. Bigg (*The Journal of the American Medical Association*, September 1, 1951) report a case of sensitivity to all forms of corticotrophin in high dilutions, as well as to other pituitary preparations. They state that the significance of allergy to corticotrophin is threefold. First, it is of practical importance because it must be taken into consideration as a hazard in this type of therapy. Secondly, it is of interest because a substance which is presumed to improve allergic manifestations is capable of giving allergic reactions. Thirdly, it is of immunological interest. It is interesting that the authors' patient had an allergic reaction on the very first injection of corticotrophin. They state that this is not in accordance with the accepted immunological principles and would suggest that this patient had previously received pituitary substances.

Herpes Zoster Appearing After Trauma.

J. V. Klauder (*Archives of Dermatology and Syphilology*, October, 1951) states that *herpes zoster* appearing after peripheral nerve injury has been frequently reported in European literature. Such occurrence is of importance in view of laws governing workmen's compensation. Of added interest is the consideration of untoward effects of trauma and possibly also factors concerned in the awakening of viruses from a condition of dormancy. In 1947 the author reported eight cases of *herpes zoster* appearing after peripheral nerve injury secondary to trauma of the skin or cornea. *Herpes zoster* with few exceptions affected the nerve supplying the region injured. The

injury to the surface of the skin or cornea was inflicted in various ways and was of variable degree. At times symptoms of sensory disturbance intervened between injury and the outbreak of *herpes zoster*. The author states that in his cases and in cases reported by others an interval of from one day to three weeks occurred from the time of injury to the appearance of *herpes zoster*; the longer the interval beyond three weeks, the greater is the probability of a non-causal role of trauma. *Herpes zoster* has been known to occur after intramuscular injections in the buttocks, lumbar puncture and osteopathic manipulation of the spine, and from deep X-ray therapy in the region of a ganglion. *Herpes zoster* may occur as an untoward reaction to arsenic. These occurrences indicate the influence of endogenous and exogenous factors in awakening viruses from a condition of dormancy.

UROLOGY.

Transthoracic Approach in Renal Surgery.

R. CHUTE (*The Journal of Urology*, May, 1951) states that the thoracoabdominal incision is of great value in certain cases of urological surgery, and 68 such cases in which operation was performed by the author and his colleagues are studied. The author states that its value lies in the remarkable wide-open exposure of the infradiaphragmatic area, particularly for difficult renal and adrenal operations. He feels strongly that this route should be chosen for nephrectomy in all cases of renal neoplasm for the following reasons: (i) The pedicle is ligated more easily, and therefore more safely. (ii) Preliminary pedicle ligation prevents the squeezing of vascular metastases into the circulation during subsequent manipulations; it also eliminates the very bothersome hæmorrhage from large veins which course over renal tumours. (iii) The surrounding perinephric fat and capsule of Gerota are easily removed *en bloc* with the kidney; they are often involved in a direct extension of the neoplasm. (iv) There is room to remove involved regional lymph glands and to remove tumour thrombi from the renal vein or the *vena cava*. (v) This incision has made possible the removal of renal neoplasms when this was found to be too difficult at the ordinary lumbar exposure. In this series the patients varied in age from one year to eighty years. The operation was performed 36 times on the left, and 32 times on the right side. There was one death, indirectly due to operation trauma and hæmorrhage, necessitating ligation of the *vena cava*. No post-mortem examination was made. There were three cases of serious complications, two of which were concerned with intrathoracic hæmorrhage.

Urinary Diversion and Cystectomy in Vesical Carcinoma.

G. T. THOMAS, D. C. MALCOLM AND A. J. BISCHOFF (*The Journal of Urology*, April, 1951) describe their experiences in the radical treatment of vesical carcinoma. They state that out of 230 cases observed at a large "tumour centre" hospital over six years, 24 patients were subjected to total cystectomy with some form of diversion of the urine. The more or less early mortality of the operation was 18%. Less than one-third of the patients lived longer than one year. The average survival time after operation for the whole group was ten months. Autopsy findings revealed that local recurrences in the true pelvis were frequent. The authors emphasize the fact that vesical cancer metastasizes early and frequently, thus refuting the widely held opinion of twenty years ago that carcinoma of the bladder could be treated as a local lesion for a long period. Metastases to bone occur frequently, and are often not recognizable in X-ray films. Most of the authors' patients' wounds healed well, but 16 of the 24 patients developed pyelonephritis. So far as obstruction in connexion with the ureteric transplants is concerned, this developed on one side in five cases, and on both sides in six cases. The authors consider that cutaneous ureterostomy should be used more often than it is; it may not be so convenient, but will ensure a longer life to many of the patients. Cystectomy is useless for carcinoma of the bladder of grades 3 and 4 and should be used only when the carcinoma is just commencing to invade the muscular wall.

Lower Nephron Nephrosis.

H. J. RIDDELL (*The Journal of Urology*, April, 1951) discusses the problem of the highly fatal lower nephron nephrosis that occurs in children, based on his experiences at a children's hospital. He states that although the condition was known several years earlier, interest was not revived until Bywaters and other British workers, in 1944, reported large numbers of cases resulting from crush injuries during the last war. The term "lower nephron nephrosis" was proposed by Lucke in 1946. In children the condition is found following transfusion reactions, severe burns, crush injuries, poisons and sulphonamide reactions. There is an initial period of shock, followed by slowly or quickly developing anuria. If there is oliguria, the little urine secreted is blood-stained, very acid, and of a fixed specific gravity of 1·010 (unaltered glomerular filtrate). There is proteinuria, with pigmented and cellular casts. With anuria there is usually hypertension, rise in non-protein nitrogen, œdema and acidosis. In some cases there may be a high serum potassium content. The mortality rate is between 70% and 90%. Pathologically there is selective destruction (necrosis) of the epithelium of the distal convoluted tubules and ascending limb of the loop of Henle. Little or no change is seen in the glomeruli. Interstitial œdema and lymphocytic infiltration are present. In patients recovering, reepithelialization occurs within two weeks of the onset. Most writers agree that the pathological changes are due to renal vasoconstriction occurring in early shock. The kidney can stand complete ischæmia for thirty minutes; if it is prolonged for two hours or more the tubular epithelium suffers severe damage. The distal convoluted tubules, as a result of the ischæmia, act like parchment so far as the glomerular filtrate, now highly acid, is concerned, and most of this filtrate diffuses back unaltered into the circulation. A falling pH of the filtrate causes precipitation of hæmatin pigment, and this mechanical blockage of the tubules aggravates the oliguria. Azotæmia occurs gradually as a result of this diffusion of the glomerular filtrate back into the circulation. In the past, the very high mortality has been due to lack of knowledge of these pathological changes. These patients were literally drowned in their own fluids in an ill-advised attempt to "dilute toxins" or to force diuresis. It is impossible for such kidneys to secrete urine until regeneration of the tubular epithelium occurs. Renal decapsulation is illogical when the œdema of the kidney is better controlled by proper management of the fluid and electrolyte intake. Extrarenal dialysis has no place in the treatment of patients with no previous renal lesion until nearly fourteen days have elapsed. The exception to this is a mounting serum potassium level. The potassium must be removed by dialysis to prevent death. As soon as oliguria or anuria is recognized, determination of the blood content of non-protein nitrogen and chloride, the carbon dioxide combining power and the serum potassium content should be made. Fluid is given in sufficient amount only to make up for insensible loss through the skin, bowel and vomitus. Glucose is given in each intravenous infusion to spare protein catabolism, and no proteins are given by mouth or parenterally. In infants the amount of fluid given is from 30 to 60 millilitres per kilogram every twenty-four hours, and even less in older children. If the diuretic phase is reached, tubular failure to reabsorb threshold substances from the glomerular filtrate may precipitate severe hypochlorœmia. Therefore, during this phase, adequate fluids and electrolytes must be given.

Retropubic Prostatectomy.

T. D. MOORE (*The Journal of Urology*, May, 1951) reviews the immediate and late results and complications in a personal series of 116 retropubic prostatectomies in which more than one year has elapsed since operation. There were two hospital deaths, making the very low mortality rate of 1·7%; 15 patients, whose average age was 75·5 years, died from various causes from two to twenty-eight months after operation. Various lesser and easily treated complications are discussed, as well as the most important, serious and troublesome of all—*osteitis pubis*. The author states that while he experienced the very high and perturbing incidence of *osteitis pubis* of 16·3% in his first 80 cases, there has been no single case of this complication in the last 79 cases. During the period of the last 79 cases the following have been the author's modifications of technique. (i) More gentle retraction of the recti muscles is practised. (ii) The prostatic capsule is now incised after the placing of hæmostatic sutures on the veins of the plexus of Santorini; this is instead of electrocoagulating them after applying artery clamps. (iii) A sharp scapel is used for incising the prostatic "capsule" instead of the electric scalpel. (iv) An aqueous solution of streptomycin is now used locally in the prostatic cavity and the entire incision. (v) An "all-out" effort is made to secure a watertight closure of the surgical capsule by means of two rows of sutures instead of one. (vi) Every "conceivable effort" is made to avoid traumatizing the pubic bone or its periosteum. The author states that the disappearance of this complication has been a most gratifying experience.

Special Articles for the Clinician.

XV.

THE EPILEPTIC CHILD.

IT is a far cry from the brief stare of *petit mal* to the prolonged twitching of *status convulsus*, from the sudden violence of a major fit to the curiously varied behaviour of a psychomotor one. Yet each is part of the pattern of epilepsy. The form of the fit in the epileptic child matters almost as much as the underlying cause and will fall into one of the following groups.

1. The major motor fit, which in its usual form consists of sudden unconsciousness, a brief tonic stage followed by violent, regular, jerking of limbs, face and body, usually some degree of cyanosis, and sometimes incontinence of urine and fæces. The fit lasts several minutes and is followed by sleep. It is not uncommon for the twitching to be more pronounced in or indeed confined to one side of the body in some fits. If this localized twitching occurs in a majority of the patient's fits, it suggests a localized area of brain damage. Occasionally the fit starts with abnormal sensations or convulsive movements in one extremity which spread centrally, consciousness perhaps being retained until the fit becomes generalized. Sometimes the fit lasts longer than the usual few minutes. In *status epilepticus* coma may last for many hours, with continuous or intermittent, localized or generalized twitching. Occasionally there is unconsciousness for many minutes before twitching occurs. A severe fit may be followed by localized paralysis that recovers in a day or so, but rarely remains as a permanent spastic weakness.

2. The minor motor fit, a very mild or incompletely developed major fit. It is short, but has essentially the same sort of components as the major fit. Often it stops before the clonic stage is reached. If twitching does occur it is brief and mild. These mild fits are among the most common seen in children. They must be distinguished from *petit mal*, for from the standpoint of treatment they are quite different.

3. The *petit mal* fit—a brief stare, a transient impairment of consciousness lasting a few seconds, with no fall, no twitching except perhaps a fluttering of the eyelids and no subsequent confusion or sleep. These fits may occur many times a day, and are common enough in childhood.

4. The myoclonic jerk, a single violent jerk of the whole or some part of the body, without unconsciousness, but sometimes followed by sleep. These fits may occur repeatedly in a day, and seem to be most common in babies with gross mental defect, though they are said to occur also in patients subject to *petit mal*.

5. The akinetic fit, in which there is a sudden violent fall of the body or dropping of the head, a momentary loss of consciousness, but immediate recovery. It is a sudden loss of postural tone in the whole or part of the body.

6. The psychomotor fit, with amnesia and oblivion to surroundings rather than unconsciousness. The duration of the fit is very variable and there may be a wide range of motor activity—undressing in public, walking into obstacles, grimacing, chewing movements, or contortion of the trunk.

7. The diencephalic or autonomic fit—sudden flushing, hiccup, sweating, pallor, tachycardia, abdominal pain, vomiting, rage or fear, without unconsciousness, but often followed by sleep, a feature of value in suggesting the diagnosis.

It is by no means uncommon for several types of fit to occur in one patient. All but the first three groups are uncommon.

Ætiology.

The disorder of brain function that causes fits may be of several types. The epilepsy may be idiopathic or essential, or it may be symptomatic of some organic brain damage. Fits may result from an illness and not occur apart from it; hypoglycæmia, acute or chronic nephritis, lead poisoning, meningitis and encephalitis are examples. Convulsions of infancy may occur only at the height of a febrile illness.

There is little question that idiopathic epilepsy is a familial disease, inherited as a recessive characteristic. Often no family history is obtained—indeed, Lennox (1945) states that "not one epileptic in five knows of any relative who was similarly affected; not one epileptic in twenty-five had an affected parent". Approximately 10% to 15% of the population have some abnormality of cerebral rhythm in an electroencephalogram. Lennox performed electroencephalographic examinations on the relatives of a group of epileptics. In only 19% were the records of both parents completely normal. Among 470 near relatives of an epileptic, approximately one-half had some degree of dysrhythmia. It is apparent therefore that though an epileptic may know of no relative with the disease, yet in his family are many with the inherited disorder of function that is potential epilepsy.

Organic brain damage of many different types can cause fits. Among children the sequelæ of cerebral birth injuries—hæmorrhage, anoxia and œdema—are quite the most common. Often some degree of mental retardation is present, and there may be some physical defect such as spastic paresis of a limb, though frequently this is not so. Congenital mental defect, progressive cerebral degenerations, brain scarring from meningitis, encephalitis, accidental injury, the irritation of cerebral tumours or cysts or a subdural collection of blood or fluid, all occasionally cause fits.

The relationship of febrile convulsions of infancy to epilepsy is of particular interest. It is not uncommon to find an epileptic among the relatives of an infant who has had such convulsions, or to find such an infant become an epileptic later in childhood. Lennox (1948), indeed, believes that the difference between febrile convulsions of infancy and epilepsy is one of degree only. When one is faced with an infant having convulsions, it is useful to have some basis for deciding whether continuous therapy for a long period is wise, and the presence of any one of the following factors would seem to justify it, for they indicate the likelihood that subsequent convulsions will occur: (i) severe, prolonged or frequent convulsions; (ii) convulsions occurring before the age of one year or after the age of four years; (iii) the occurrence of convulsions without an obvious precipitating illness; (iv) a family history of epilepsy; (v) an abnormal electroencephalogram; (vi) any suspicion of mental defect or organic brain damage.

Any type of fit may occur in either idiopathic or organic epilepsy, but in general *petit mal*, psychomotor fits, akinetic fits and autonomic fits are most commonly idiopathic, while focal major fits and myoclonic jerks are most often an expression of brain damage. Generalized major fits are common in both groups.

It is important to remember that in the epileptic of any type certain influences may precipitate fits. Such influences are febrile illness, emotional tension, a sudden shock, and physiological disturbances such as menstruation.

Intelligence and Behaviour.

The greatest tragedy of epilepsy in children is not the fits, but the retarded intelligence and abnormal behaviour that not infrequently accompany the disease. It is difficult to estimate what proportion of epileptic children are mentally retarded, for impressions and data obtained from hospital and consultant practice are misleading because of the relatively high proportion of serious or difficult cases encountered. Of the children attending the Seizure Clinic of the Royal Alexandra Hospital for Children, Sydney, 25% are mentally retarded. It is probable that there is some mental defect in one-fifth of the children subject to fits. The majority are certainly of normal intelligence, and a few distinctly superior.

A number of factors contribute to the impaired mentality. Quite the most important is brain damage that existed before the fits occurred, the result of congenital mental defect or birth injury, and much less commonly of encephalitis, meningitis, hydrocephalus, or cerebral degenerations. These children were subnormal before they had epilepsy. The fits and the mental defect are but symptoms of the underlying disease. The behaviour of such children varies greatly. They may be docile, cooperative and pleasant, or they may be restless, destructive, wilful or vicious, a tremendous burden to those who must care for them.

A second factor is that of inheritance. It seems certain that there is some genetic link between epilepsy and mental defect. There are more subnormals among the relatives of epileptics than among the general population, and the child may have inherited a mind of poor quality.

A third factor is the influence of repeated seizures. Sometimes fits cannot be controlled, and while an occasional convulsive seizure is unlikely to cause mental deterioration, frequently recurring major fits certainly will (Bridge, 1949). This degeneration is roughly proportional to the frequency, severity and duration of the fits, and becomes the greatest cause of mental defect in adult epileptics.

Fourthly, the continued use of large doses of sedative drugs may dull the mind.

Finally, the disease may cause emotional stress and unbalanced attitudes in the parents and the patient himself that seriously hamper his normal behaviour.

The Electroencephalogram.

Electrical impulses arise continually in the brain of every individual and can be recorded by the electroencephalograph. In normal people the recorded waves are regular and of low voltage. They are slower and rather less regular in young children than in older children or adults. Several types of dysrhythmia may be found in epilepsy. The commonest consists of irregular runs of slow high-voltage waves. The spike and wave, slow and of high voltage, is often seen and is highly significant. It is most characteristic of *petit mal*, and if a recording is obtained during a *petit mal* seizure the tracing may consist entirely of regular slow spikes and waves. However, scattered spike and wave forms may be found in any type of epilepsy in childhood. The very rapid, very high voltage spikes of the *grand mal* attack are rarely seen. It is only occasionally that a burst of such waves is recorded in the interval between fits.

The electroencephalogram is a useful adjunct in the management of epilepsy. It helps to establish a diagnosis, for sometimes it is not easy to tell from a parent's description whether one is dealing with a simple breath-holding turn or a minor motor fit, with hysteria or psychomotor epilepsy. It is true that occasionally a normal tracing will be found in a severely epileptic subject, and that abnormal tracings are found in many people who never take fits. The electroencephalogram is therefore not a final arbiter. Like most diagnostic aids, it must be considered together with the evidence from the age-old sources of history and examination. It is of similar value in detecting or confirming a localized brain lesion. The abnormal waves may arise in this area alone, or if they are generalized they may be more pronounced in this area. The electroencephalogram helps too in assessing progress of any patient, for in many epileptic children who respond well to treatment, the electroencephalogram gradually becomes normal. It has provided evidence of the genetic background of epilepsy. It has revealed among apparently normal people many with the dysrhythmia that indicates potential epilepsy, and these particularly among the relatives of epileptics. It has demonstrated therefore that there are vastly different degrees of this disease. People will think of epilepsy in a different way and with less terror if they realize that it is a very widespread and usually a very mild disease.

Diagnosis.

There are several steps in the diagnosis of epilepsy. First one must decide whether the turn described is a fit or simply a vasovagal faint, a breath-holding turn, a temper tantrum or an act of hysteria. Secondly, it must be decided what type of epileptic fit occurs. Thirdly, the underlying cause, essential epilepsy or organic brain damage, must be considered. If it is organic brain damage, one must ask whether an old and stable lesion is present, or a growing and active one, such as a tumour that demands treatment other than anticonvulsant drugs. Fourthly, the degree of physical and mental impairment must be approximately assessed. Finally, the psychological adjustment of patient and family to the disease must be considered.

Other investigations are of value in some cases. The pneumoencephalogram helps demonstrate local brain lesions, but it should be reserved for those cases in which it is suspected that surgical measures may be necessary or of value. Radiological examination of the skull is wise when there is doubt of the ætiological basis, or when trauma or intracranial pressure is suspected. Determination of the blood sugar content, the use of the Wassermann or Mantoux test, or examination of the cerebro-spinal fluid is occasionally indicated.

Treatment.

The treatment of epilepsy depends very largely on the use of anticonvulsant drugs. In their use there is one essential aim, and one only: to stop fits without producing toxic symptoms. It follows that the correct dose for any patient is the dose that is needed to control his seizures, as long as unpleasant or dangerous side effects are not being produced, and this varies widely in different subjects. Decide the type of fit; choose the drug that is usually safe and effective for its control; start with a reasonable dose, and if control is not achieved increase the dose at intervals till the limit of tolerance is reached; if fits still occur supplement or replace the drug with another. The right dose of the right drug is being given only when maximum benefit is being achieved.

Phenobarbital is of some value against all types of fit. It is very well tolerated by children, and there is usually a wide margin between therapeutic and toxic levels. A reasonable initial dose varies from one-sixth of a grain three times a day for a baby to half a grain for a big child. Initial drowsiness may result, but this usually passes after a week or two. Drowsiness and staggering are the toxic symptoms that limit dosage. Occasionally intense irritability and excitement or a morbilliform rash occurs, and if it does the drug should be abandoned.

Phemitone ("Prominal" or "Mebaral", n-methylethylphenyl barbituric acid) is similarly of some value against all types of seizure. Drowsiness is its limiting factor, and there is much less margin between therapeutic and toxic levels than with phenobarbital. Some patients do better with phenobarbital and some with "Prominal", but the drugs are essentially interchangeable. An average dose is half a grain twice daily for an infant to two grains three times daily for a big child.

"Dilantin" or phenytoin (sodium diphenylhydantoinate) is usually the most effective drug against major and minor motor fits and may be of benefit in all except *petit mal*. This it may aggravate. However, if *petit mal* is diagnosed and other drugs fail to give benefit, "Dilantin" should be tried. It is occasionally a matter of extreme difficulty to distinguish between *petit mal* and a mild minor motor or psychomotor fit, and this may be why "Dilantin" occasionally seems to control what has been regarded as *petit mal*. The drug is dispensed in capsules ("Dilantin") or tablets (phenytoin) of half a grain and one and a half grains. An average dose is half a grain twice daily for an infant to one and a half grains three times daily for a big child. The usual signs of overdosage are ataxia and tremor, which occur promptly when too much is given, and usually at a level of dosage very little above the best therapeutic figure. Hypertrophy of the gums may occur gradually and can be relieved by good mouth hygiene and massage of the gums. It necessitates changing the drug only if it is very severe. Gastric distress may occur, but is usually relieved by taking the drug with meals or a large drink. I think "Dilantin" was the cause of a hæmatemesis in one child patient of mine. A morbilliform, hæmorrhagic or rarely exfoliative rash may occur and necessitate omission of the drug. If it is not severe and disappears promptly when the drug is withdrawn, careful reintroduction may be attempted if other drugs will not give the same benefit. This applies particularly to the *erythema multiforme* that may occur ten days or so after "Dilantin" has first been given. It is often useful to combine "Dilantin" with phenobarbital or "Prominal".

"Tridione" (trimethyloxazolidine-dione) is usually the most and often the only effective drug in *petit mal* and may be of use in akinetic and myoclonic epilepsy. It is dispensed in tablets of 0·15 gramme and in capsules of 0·3 gramme. An average dose is 0·15 gramme three times daily for a small child and 0·3 gramme for a big child. The danger of the drug lies in the real risk of depression of bone marrow activity. This affects the neutrophile leucocytes first, but after a few weeks the red cells and platelets fall and fulminating pancytopenia results, with the likelihood of a purpuric rash or bleeding, gross anæmia, agranulocytosis with uncontrolled infection and a great probability of death. If "Tridione" is used, a leucocyte count must be carried out fortnightly for the first six weeks, then monthly for a year, and then about each three months. In 80% of cases Abbott and Schwab (1950) report that the blood remained unchanged. In 20% a "controlled neutropenia" occurs, the neutrophile cells falling below 3000 per cubic millimetre, but not low enough for dangerous clinical symptoms to occur. Davis and Lennox (1947) report definite neutropenia in 6·3% of patients and borderline changes in a further 7%, and conclude that if the neutrophile cell count falls below 2500 per cubic millimetre it should be checked more often than monthly, and if it falls below 1600 per cubic millimetre therapy should be withheld. Other toxic effects are erythematous or urticarial or occasionally severe exfoliative rashes, photophobia, gastric distress, nervousness or behaviour problems. Occasionally nephritis of the nephrotic type has resulted, and once corneal erosion occurred as part of an exfoliative dermatitis. Despite these dangers, "Tridione" if carefully controlled is a very valuable drug. It should not be given to patients who are isolated or irresponsible and will not report for regular control. Nor should it be given to the patient whose fits are controlled by phenobarbital or "Prominal".

"Phenurone" is said to be the most effective drug for psychomotor fits, but it is not yet available in Australia.

It may cause personality changes, especially excitability and talkativeness, and rarely rashes, albuminuria and hepatitis. "Mesantoin" has actions similar to "Dilantin", but may cause the same blood and skin changes as "Tridione". "Paradione" has the same effect as "Tridione", but occasionally succeeds when "Tridione" fails. Bromides are still of some value for an occasional patient who is difficult to control with other drugs. The alleged anticonvulsant properties of "Dexedrine" and caffeine are quite unimpressive, but these drugs are sometimes a help to combat the drowsiness caused by large doses of sedatives.

When several types of fit occur more than one drug can be used. Even "Dilantin" and "Tridione" can be used together in the treatment of the patient having *petit mal* and major fits.

Surgical treatment plays a small part in the management of epilepsy. It is indicated when there is a progressive lesion such as a tumour, or when the fits arise from a clearly localized and accessible area of brain damage and are not controlled by adequate trial of drugs.

The general hygiene and psychological management of the patient are important. Any impairment of general health should be remedied. His intellectual and phyical capacity should be considered and suitable education and vocational training arranged. Excessive anxiety and harmful overprotection by the parents should be corrected. The child should be taught to avoid dangerous situations, and should be helped to adopt a sane, balanced, optimistic attitude to his disease and to life, for in most cases this is amply justified.

Prognosis.

The outlook is essentially good. In most cases the fits can be controlled, and it is certain that if seizures are controlled for two or three years, drug treatment can be gradually omitted and fits usually do not return. The electroencephalogram improves and often returns to normal. Epilepsy in the majority of children is a curable disease.

However, this is not always so. In some cases the control is only partial, and in some the fits seem to be unresponsive to treatment. The most difficult patients are those with organic brain damage who are taking fits of several types, and about one-fourth of the patients with *petit mal*. It is hoped that new drugs now being developed will improve the management of such seizures. Uncontrolled fits, especially major fits, cause progressive mental deterioration, and at present the outlook of these patients is bad.

D. G. HAMILTON,
Sydney.

References.

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British Medical Association News.

A BRITISH MEDICAL ASSOCIATION PRIZE (ANNUAL GENERAL MEETING, 1935).

IN December, 1936, the General Executive of the 1935 Annual General Meeting of the British Medical Association resolved that the balance of the surplus funds should be given to the Council of the Victorian Branch of the British Medical Association for investment in approved securities with the suggestion that the income therefrom should be used for a triennial prize for original work in medicine or the allied sciences. The prize would be open to all members of the Association in Australia and its Mandated Territories and in New Zealand, and to any graduate of an Australian university who was a member of this Association. The details of this proposal were to be elaborated by a committee appointed by the Council of the Victorian Branch.

This gift was accepted by the Council and a prize committee was appointed by the Council to act on the above suggestion and elaborate the details.

This prize has not been awarded previously because of the desire of the committee to allow the capital sum to accrue by investment, and also by the intervention of war.

The prize committee appointed by the Council of the Victorian Branch has decided on the following conditions:

The prize is open to all members of the Association in Australia and its Mandated Territories and in New Zealand, and to any graduate of an Australian university who is a member of the Association.

The prize is to be awarded for that contribution towards the study of problems in the medical and allied sciences adjudged to be of greatest merit. If no contribution be considered to be of sufficient merit, the prize may not be awarded.

The prize shall consist of a gold medal suitably inscribed, together with the balance of the income from the capital fund available for distribution at the time.

The period during which any contribution for consideration may be made shall be the three years ending on December 31 immediately preceding a meeting of Congress.

This is a triennial prize, and it is intended that it may be awarded for the first time at the meeting of Congress to be held in Melbourne in August, 1952. To minimize the risk that a contribution of high value may be overlooked, it will be appreciated if the contributor of any such work complying with the above conditions be nominated to the prize committee. It is requested that such nominations be forwarded not later than April 30, 1952, to Dr. J. P. Major, Chairman of the Prize Committee, British Medical Association (Victorian Branch), 426 Albert Street, East Melbourne, C.2, Victoria.

Medical Societies.

THE MEDICAL DEFENCE SOCIETY OF QUEENSLAND.

ANNUAL MEETING.

THE annual meeting of the Medical Defence Society of Queensland was held at British Medical Association House, 225 Wickham Terrace, Brisbane, on Wednesday, February 27, 1952, at 4.30 p.m., the President, Dr. Neville G. Sutton, in the chair.

Annual Report of Council for 1951.

The annual report of the Council for the year ended December 31, 1951, was presented and adopted. The report is as follows.

The Council has pleasure in presenting the fiftieth annual report of the Medical Defence Society of Queensland for the year ended December 31, 1951.

Membership.

The society has now a membership of 551, as against 547 last year. During the year 26 new members were elected, and two were reinstated.

Our losses were: deceased 7, resigned 8, left the State 9.

Obituary.

It is with much regret that we record the deaths of the following members: Dr. Gavin H. Cameron (who was a member of the Council for a number of years and died in August last), Dr. K. F. C. Brunnich, Dr. John Crawford, Dr. Milton Geaney, Dr. Charles E. S. Jackson, Dr. R. Martin Smith, Dr. Eric J. Davies.

Office Bearers and Council, 1951.

The following office bearers were unanimously reelected by the Council: *President*, Dr. Neville G. Sutton; *Vice-President*, Dr. G. W. Macartney; *Honorary Treasurer*, Dr. T. V. Stubbs Brown; *Honorary Secretary*, Dr. R. G. Quinn; *Councillors*, Dr. Gavin H. Cameron, Dr. H. W. Horn, Dr. F. W. R. Lukin, Dr. H. Masel, Dr. Athol Quayle, Dr. F. Garrett Scoles, Dr. J. G. Wagner.

Dr. H. W. Horn, Dr. F. W. R. Lukin and Dr. J. G. Wagner, who retired in conformity with the by-laws, were reelected to the Council.

Medico-Legal.

Three cases were submitted to the society during the year. One appears to have been dropped, one is still pending, and the third was settled out of court, the Medical Protection Society, Limited, contributing to the amount involved.

Indemnity Insurance: Medical Protection Society, Limited.

The arrangement which exists between the Medical Defence Society of Queensland and the Medical Protection Society, Limited, London, has continued to work very satisfactorily during the year. Of the 551 members, only 13 have indemnity insurance with other approved corporations.

Finance.

It will be shown from the balance sheet that the net surplus for the year ended December 31, 1951, amounted to £326 7s. 4d.

Some items of income and expenditure are as follows:

	£	s.	d.
Receipts—			
Annual subscriptions to the Medical Defence Society	292	12	0
Entrance fees	27	6	0
Subscriptions, indemnity insurance	2558	13	9
Interest:			
Commonwealth Government Treasury Bonds and Inscribed Stock	229	2	2
Commonwealth Savings Bank	10	14	4
Expenditure—			
Amount remitted to Medical Protection Society, Limited	2547	17	10
Secretarial and clerical assistance	204	0	0
Auditor	17	17	0
Rent, postage, bank charges, printing and stationery	32	10	11
Legal expenses	6	16	6
Federal income tax	23	8	0

The total assets of the society are £8345 13s. 7d.

An amount of £7170 is invested in Commonwealth Inscribed Stock.

Current assets include bank balances and cash amounting to £1176 14s. 1d., portion of which is to be invested in Commonwealth Government Inscribed Stock.

NEVILLE G. SUTTON,
President.

Balance Sheet and Financial Statement.

The balance sheet and financial statement for the year ended December 31, 1951, was adopted.

Election of Councillors for 1951.

The following members, who had retired in accordance with the by-laws, were reelected: Dr. G. W. Macartney, Dr. R. G. Quinn, Dr. F. Garrett Scoles. Dr. Roy Biggs was elected to fill a vacancy on the Council.

Election of Auditors.

Messrs. R. G. Groom and Company, Chartered Accountants (Australia), were reelected auditors for the ensuing year at a remuneration to be fixed.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

DEATH OF SERJEANT AITCHISON.[1]

[*The Monitor*, Sydney, January 13, 1827.]

We understand that of Apoplexy there are four kinds, and that Serjeant Aitchison died of the kind called "SANGUINA". And we are further given to understand that, if INSTANT relief be afforded, the patient may recover of the sanguina apoplexy. In Aitchisons case, one hour transpired between the fit and the presence of the first medical man. Hence it follows that if the medical Gentleman first sent for, had INSTANTLY gone down, there would have been much more chance for AITCHISON'S life, than there could possibly be when the second person, who was applied to, arrived.

[*The Australian*, January 6, 1827.][1]

[CONDENSED.]

A Coroners Inquest was summoned on Thursday last (4th instant) on the body of ELIJAH AITCHISON Serjeant of the 3rd Regt or Buffs who died suddenly.

He took ill at his home and Dr IVORY surgeon to the Regiment who was sent for, without seeing him, ordered his removal by "four fatigue men" to the Military Hospital. Meantime DR CONNOLLY who had also been summoned visited his home and found the Serjeant dead. Dr Ivory in evidence stated that death was due to an apoplectic seizure —this he had confirmed by a postmortem examination— and that no medical treatment would have been of any avail.

Dr. Connolly stated that death was due to an apoplectic or epileptic seizure: that if medical aid had been obtained in time deceased would have recovered: that bleeding, simply, if resorted to in time, would have been a restorative. He had been a military surgeon for some years but could not reconcile the idea of neglect being evidenced towards any individual however low his rank or situation in life might be.

Some of the jurors expressed the view that the surgeon to the Regt had accelerated AITCHISON'S death by not attending when first sent for.

Both doctors were recalled: Ivory was allowed to cross examine Connolly who refused to answer questions. There were heated exchanges between the doctors and between members of the jury and either of the doctors—a third practitioner whose opinion was sought concurred with Ivory.

The coroner directed the jury thus—The evidences of three medical men are before you: they are unanimously of opinion that the deceased died a natural death. To this same conclusion gentlemen I think you will be bound to arrive, whatever negligence may appear to you to have been betrayed by anyone: this is a subject for future investigation.

Verdict—Died by Visitation of God.

[1] From the original in the Mitchell Library, Sydney.

Correspondence.

NASAL SINUSITIS.

SIR: In your issue of March 1 Dr. Blashki is very critical of a general practitioner who, worried at the thought of sending a patient with allergic sinusitis to an ear, nose and throat specialist, attempted treatment himself, using short-waves and penicillin. This, of course, is wrong treatment, and I do not hold with it, because the first line of approach in the treatment of allergic sinusitis is to withdraw or deal with the offending allergens.

However, Dr. Blashki falls into the same error as the general practitioner when he extols the virtue, even claiming a cure, in using a surgical approach as a single measure of treatment. This claim is designed to give the impression that the mere boring of a hole into the antrum cavity is sufficient to effect a cure of an allergic sinusitis. It is this approach and the damage caused by surgery in the past which has filled the mind of the general practitioner and others with fear at the thought of referring his patient to the surgeon.

No less a person than C. Gill-Carey, surgeon of the Royal National Throat, Nose and Ear Clinic, and Dean of the Institute of Laryngology and Otology, states in the *British Medical Journal* of February 18, 1950, that "during the past twenty years, sinusitis has become a medical rather than a surgical disease".

Not a week passes without I see a patient who has had irreparable damage done to his sinuses by surgery. It is a sorry sight, and medical men can be numbered appreciably among the victims. Some years ago, when a general practitioner, I had a visit from a doctor convicted of a drug offence, who pleaded with me to give him six grains of morphine. I asked what precipitated his morphinism, and

[1] From the original in the Mitchell Library, Sydney.

he replied that he suffered such intense facial pain following surgery to his sinuses that the only relief he could obtain was from morphine injections. Another, since dead, who contributed frequently to these columns, told me he was taking morphine daily following surgery to his ethmoid sinuses by one of the leading surgeons in America. Another in the vanguard of his specialty confessed that had it not been for his children and his religion he would have taken his life years ago because of pain following a sinus operation. I lost a friend, a promising graduate of two years' standing, who journeyed to Vienna and died as the result of sinus surgery.

At the risk of offending the reader who may dislike mixing scriptural quotations with medical literature, I shall quote what I think is appropriate to the problem:

> And a certain woman, which had an issue of blood twelve years, and had suffered many things of many physicians, and had spent all that she had and was nothing bettered, but rather grew worse . . . touched his garment.

If the sufferings (the inspiration for Dr. Blashki's letter) of the patient submitted to diathermic treatment were impressive to the mind of Dr. Blashki, they would in my opinion be nothing to the sufferings of many patients who have had sinus surgery.

Short-wave therapy using the rotating electrode which I employ is the only instrument or measure which I know that will relieve the intolerable pain associated with sinus disease. It promotes secretions and shrinks mucosal hyperplasia providing due attention is paid to ætiological conditions. I do not think it causes any damage provided it is used correctly. I believe if failures result with conservative treatment of sinus disease, using short-waves as complementary treatment, then such failures are due to either an inadequate appreciation of the problem of sinus disease, to failure of the patient to cooperate or to irreversible tissue changes in the sinus mucosa.

If the surgeon can produce to me just one case of chronic sinus disease which conservative treatment such as I employ failed to cure, and which has subsequently yielded to surgical procedure and a cure effected, then I shall make full admission through these columns that I have wrongly judged the position.

Yours, etc.,

Sydney,
March 4, 1952.

WILKIE SMITH.

A "STERLING AREA PHARMACOPŒIA".

SIR: It seems that we live in a world of crisis, and one of the crises of which we hear a great deal concerns the dollar.

It is possible that the British Medical Association could make a contribution to the alleviation of this particular problem by issuing a "Sterling Area Pharmacopœia". Perhaps the Government, too, could make a contribution by producing such a volume as a guide for those prescribing in its own institutions.

Yours, etc.,

12 Collins Street,
Melbourne,
March 5, 1952.

D. F. LAWSON.

SUBACUTE BACTERIAL ENDOCARDITIS CAUSED BY ERYSIPELOTHRIX RHUSIOPATHIÆ.

SIR: *Re* "Subacute Bacterial Endocarditis Caused by Erysipelothrix Rhusiopathiæ", published in THE MEDICAL JOURNAL OF AUSTRALIA of March 8, 1952.

One read with great interest the report of the above case. One would venture to suggest, however, that the diagnosis is open to serious criticism. From the history given there is little doubt that the patient was suffering from a septicæmia superimposed on a preceding rheumatic condition. That he was not suffering from a subacute bacterial endocarditis caused by the microorganism recovered from the blood-stream is strongly suggested on several counts:

1. Lewis states that one of the cardinal signs of a subacute bacterial endocarditis is the pronounced pallor of the patient. In this case "the patient looked healthy". One has yet to see a case of subacute bacterial endocarditis that did not look extremely ill, anxious and pallid.

2. Another cardinal sign of this condition is clubbing of the fingers, which was not mentioned in this patient's case history.

3. A third cardinal sign of the greatest importance, namely, the occurrence of either systemic or pulmonary emboli, was conspicuous by its absence in this case.

4. Possibly because there was no temperature chart shown to indicate the time reaction of this patient to penicillin, one got the impression, probably quite erroneously, that he reacted too smoothly and easily to penicillin for the condition to be compatible with a true subacute bacterial endocarditis.

5. Again, the history of this case suggests that the condition was acute and not subacute, as he was ill apparently for only a week before admission to hospital with a temperature of 100·4°. Surely the usual picture of a subacute bacterial endocarditis shows a more prolonged approach, with a spiky temperature chart from time to time and small bouts of pyrexia for weeks or months before the higher and more consistent temperature readings show, with other clinical findings, the real nature of the disease, if this has not already been diagnosed.

6. One would like to ask Dr. Lawes how the diagnosis of a patent interventricular septum was arrived at, still bearing in mind that the patient looked healthy.

One would like to suggest that a more correct diagnosis in this case is "an *erysipelothrix rhusiopathiæ* septicæmia associated with a preceding rheumatic carditis".

Yours, etc.,

Grace Building,
77 York Street,
Sydney.
March 12, 1952.

W. E. DAVID.

Congress Notes.

AUSTRALASIAN MEDICAL CONGRESS (BRITISH MEDICAL ASSOCIATION).

THE Executive Committee of the Eighth Session of the Australasian Medical Congress (British Medical Association) to be held at Melbourne from August 22 to 29, 1952, has sent the following information for publication.

Visual Aids.

The Executive Committee of Congress has planned to take full advantage of the outstanding work in visual aids being carried out at the University of Melbourne under the direction of Mr. Newman Rosenthal, B.A., B.Sc., who has been made an honorary member of Congress for his cooperation and interest in the Eighth Session. On Tuesday, August 26, there will be a demonstration of the latest advances in visual aids as applied to medical practice, and an exhibition (which will be open all day) has been arranged for Wednesday, August 27. This phase of Congress activities should be one of the most interesting scientific features of the week.

Another attraction of the Eighth Session will be the presentation of the latest scientific and documentary films each day. Films relating to the papers discussed at sectional meetings will be shown at different theatres throughout the university from 12 noon to 1 p.m. and from 4 p.m. to 5 p.m., and documentaries of general interest will also be screened every day at the Union Theatre. One of the most topical of these should be the film on atomic burns made by the Air Force, which will be shown after the combined meeting on "The Mass Management of Burns" to be held on Wednesday morning, August 27, under the chairmanship of Sir Samuel Burston.

Congresses.

INTERNATIONAL CONGRESS ON MEDICAL LIBRARIANSHIP.

IT is proposed to hold an International Congress on Medical Librarianship in London in July, 1953. Sir Cecil Wakeley, K.B.E., C.B., President of the Royal College of Surgeons of England, has kindly consented to accept the honorary presidency of the Congress. The programme will include formal sessions for reading and discussion of papers, visits to medical libraries and social functions. It is hoped also to have in connexion with the Congress an exhibition of medical books and periodicals and library equipment. All

those actively engaged or interested in medical librarianship throughout the world are invited to participate. Requests for further information may be addressed in advance to the Honorary Secretary, First International Congress on Medical Librarianship, c.o. The London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1.

Medical Practice.

THE CONTROL OF LIFE-SAVING DRUGS.

THE following statement by Sir Earle Page, Federal Minister for Health, is published at the request of the General Secretary of the Federal Council of the British Medical Association in Australia.

The critical emergency brought about by the wide restriction of imports into Australia from all countries in order to avert bankruptcy of the sterling area calls for prompt action by the medical profession to enable the best advantage to be obtained for the public from the limited quantities of life-saving drugs that may be available.

The Federal Government desires that the control necessary for this purpose should, as far as possible, be exercised by the profession itself.

In February last, before this acute emergency arose, the Federal Council of the British Medical Association had indicated its decisions to assist in the matter of controlling unnecessary prescribing and abuse of life-saving drugs. The Government has accepted these decisions, and will implement them to the full in cooperation with the British Medical Association.

On February 8, 1952, also before this critical emergency, the Antibiotics Committee of the National Health and Medical Research Council recommended, *inter alia*, that the issue of antibiotics, other than penicillin, be controlled by the Commonwealth Department of Health in each State who will consult with a member of the State Antibiotics Committee in cases where the indications for their use are not clear.

In order to achieve immediate results, the Government is limiting the use of various antibiotics to those diseases for which they have been proved effective specifics. The list of these diseases will be under continual review by the Antibiotics and Life-Saving Drugs Advisory Committees. Medical practitioners may not prescribe antibiotics as pharmaceutical benefits for other than these specified diseases before they have consulted with special antibiotics committees set up by the British Medical Association in each region of the State. Where possible, these committees will act with the Commonwealth medical officer at the Commonwealth Health Laboratory, who will be able to do sensitivity tests. The necessary administrative machinery for the operation of this procedure will be prepared in collaboration with the British Medical Association.

The Department of Trade and Customs has announced that the licensing position of drugs and chemicals will be a 40% cut for drugs and chemicals n.e.i. when not packed for retail sale, and an 80% cut for all other drugs, chemicals and medicines. The import quota on which the percentage cut will work is based on the year 1950-1951, when the imports of some antibiotics were very small.

It is obvious that a case for favourable discrimination for such medicines cannot be made unless adequate measures have been taken to curtail the prescribing of these drugs for the diseases for which they are specific.

The Government is also very disturbed on another aspect of this matter. The use of potent antibiotics as the first choice for common and ordinary ailments is encouraging the emergence of a race of resistant organisms precluding their effective use in serious crises. Also, greater and greater doses will be needed as germs grow more resistant. This will add enormously to the cost to the Government, but, more important still, these drugs will lose their life-saving significance and become useless in those infections for which they are specific.

To avert this catastrophe, as well as to help in the national crisis, the whole-hearted and intelligent cooperation of the medical profession is requested in the control of potent antibiotics at this critical stage.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED MARCH 15, 1952.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	..	..	..	..	..	..	..	..
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	..	..	..
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	1(1)	1	..	..	..	..	..	2
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	..	..	4(2)	..	..	1	..	..	5
Diphtheria	2(1)	9(7)	3(2)	3(2)	2(2)	..	..	..	19
Dysentery (Bacillary)	..	1	1(1)	1	2(2)	..	..	2	7
Encephalitis	..	1	..	..	..	..	..	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	..	..	..	..	20(6)	..	..	..	20
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	3	..	..	..	..	..	3
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	1(1)	2(1)	..	..	..	1	..	..	4
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	3	3(2)	3(1)	21(10)	..	3	..	..	33
Puerperal Fever	..	..	2(1)	..	..	..	1	..	3
Rubella	..	..	..	..	..	..	..	1	1
Salmonella Infection	..	..	..	..	..	..	..	2	2
Scarlet Fever	23(3)	24(15)	2(1)	1	1	10(1)	..	..	61
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	2(2)	..	1(1)	..	..	..	3
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	33(26)	14(1)	12(5)	13(8)	10(6)	2	..	2	86
Typhoid Fever	..	1(1)	2(2)	..	1	..	..	..	4
Typhus (Flea-, Mite- and Tick-borne)	..	..	1	..	1(1)	..	..	..	2
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Naval, Military and Air Force.

APPOINTMENTS.

THE following appointments, promotions *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 19, of February 28, 1952.

NAVAL FORCES OF THE COMMONWEALTH.

Citizen Naval Forces of the Commonwealth.

Royal Australian Naval Reserve.

Appointments.—Dennis Thorman Shortridge is appointed Surgeon Lieutenant-Commander, dated 18th September, 1951. Kenneth Rothwell Barder is appointed Surgeon Lieutenant, with seniority in rank of 12th February, 1948, dated 17th October, 1951.

ROYAL AUSTRALIAN AIR FORCE.

Permanent Air Force.

Medical Branch.

The following are appointed to short-service commissions, on probation for a period of twelve months, with the rank of Flight Lieutenant: James McLean Morrison (036133), 2nd January, 1952, Ronald Grahame Hall (024849), 3rd January, 1952, Reginald William Lewis Hall (024941), 10th January, 1952.

Air Force Reserve.

Medical Branch.

Flying Officer A. N. Turner (407344) is transferred from the General Duties Branch, 17th November, 1951, with the rank of Flight Lieutenant.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Clinical Meeting at Balmoral Naval Hospital.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that a clinical meeting will be held at the Balmoral Naval Hospital on Tuesday, April 22, 1952, at 2 p.m., when Dr. F. F. Rundle will speak on "Some Modern Concepts in Abdominal Surgery". Clinical cases will be shown at 4 p.m., after afternoon tea. All members of the medical profession are cordially invited to attend.

University Intelligence.

THE UNIVERSITY OF MELBOURNE.

Beattie-Smith Memorial Lectures on Insanity.

THE eighteenth Beattie-Smith Memorial Lectures on Insanity will be delivered by Dr. Barry Mulvany in the Anatomy Theatre, University of Melbourne, at 8.15 p.m. on May 5 and 12, 1952. The subjects of the lectures will be, respectively, "Psychiatry, the State and the Individual" and "Depressive Mental Illness". Both lectures are open to all members of the medical profession.

Obituary.

JAMES VERE ARKLE.

WE regret to announce the death of Dr. James Vere Arkle, which occurred on March 20, 1952, at Perth.

FRANCIS JOHN NIALL.

WE regret to announce the death of Dr. Francis John Niall, which occurred on March 22, 1951, at Kew, Victoria.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Dignam, Phyllis, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Harbison, Ronald George, M.B., B.S., 1950 (Univ. Sydney), Sydney Hospital, Sydney.

Rigg, Charles Andrew, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Diary for the Month.

APRIL 14.—Victorian Branch, B.M.A.: Finance Subcommittee.
APRIL 16.—Western Australian Branch, B.M.A.: General Meeting.
APRIL 17.—New South Wales Branch, B.M.A.: Clinical Meeting.
APRIL 17.—Victorian Branch, B.M.A.: Executive Committee.
APRIL 18.—Queensland Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

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